

# NIH Public Access

**Author Manuscript** 

Alcohol Clin Exp Res. Author manuscript; available in PMC 2014 December 01.

Published in final edited form as:

Alcohol Clin Exp Res. 2013 December ; 37(12): . doi:10.1111/acer.12191.

## A daily process examination of the bidirectional relationship between craving and alcohol consumption as measured via Interactive Voice Response (IVR)

Tera L. Fazzino, MA $^{1,2,^{\ast}}$ , Valerie S. Harder, MHS, PhD $^2$ , Gail L. Rose, PhD $^2$ , and John E. Helzer, MD $^2$ 

<sup>1</sup>Department of Psychology, University of Vermont, 2 Colchester Avenue, Burlington, VT 05401, USA

<sup>2</sup>Department of Psychiatry, University of Vermont, 1 South Prospect Street, Burlington, VT 05401, USA

## Abstract

**Background**—Craving is a central component to alcohol use disorders, although there are contradictory findings in the literature regarding the importance of craving in alcohol use. The study goal was to examine the daily occurrence of craving and the bi-directional relationship between craving and alcohol consumption in heavy drinkers.

**Methods**—Participants received brief alcohol interventions from their primary care physicians and then were asked to make daily reports of craving and alcohol consumption to an interactive voice response (IVR) telephone system for 180 days. The study sample included 246 participants (166 men) with mean age of 46. Ninety-seven percent were Caucasian and 66% met criteria for alcohol dependence.

Analysis used generalized estimating equations (GEE) to evaluate whether craving intensity predicted next day alcohol consumption and whether alcohol consumption predicted next day craving intensity. Significant interactions with gender led to stratified analyses.

**Results**—GEE analyses revealed a significant bi-directional relationship between craving and drinking, where craving intensity predicted next day total drinks consumed (p=.001), and total drinks predicted next day craving intensity (p=.02). Exploratory analysis found that gender significantly moderated the craving-drinking relationship (p=.002) with males increasing next day alcohol use more (b=.19) than females (b=.08).

**Conclusions**—Findings suggest a bi-directional relationship between craving and drinking may contribute to the development or maintenance of heavy drinking, particularly for males. Based on our findings, we recommend that during brief interventions, physicians address both drinking and craving and provide advice for coping with craving.

## Keywords

Alcohol; craving; gender; interactive voice response

<sup>&</sup>lt;sup>\*</sup>Corresponding Author: Health Behavior Research Center Department of Psychiatry University of Vermont UHC Campus 4570H3 1 South Prospect Street Burlington, VT 05401 USA tfazzino@uvm.edu.

## Introduction

Craving is a central component in alcohol use disorders and many individuals who are dependent on alcohol experience craving (American Psychiatric Association, 1994; de Bruijn et al., 2004). Craving is defined as a strong subjective urge to use the substance (American Psychiatric Association, 1994) and has been hypothesized to occur from physiological and conditioned withdrawal (Drummond et al., 1990). The importance of craving has been recognized by the American Psychiatric Association, which proposed adding craving as a new diagnostic criterion for alcohol dependence in the fifth edition of the Diagnostic and Statistical Manual (DSM-5) (Jones et al., 2012). Additionally, coping with craving is a focus in many forms of treatment for alcoholism, including cognitive behavioral therapy and cue exposure therapy (Loeber et al., 2006).

Cross-sectional studies evaluating the relationship between craving and alcohol consumption have obtained mixed results. Some researchers examined craving in patients enrolled in standard inpatient or outpatient alcohol treatment and found that craving pre-treatment (Bottlender and Soyka, 2004), during (Gordon et al., 2006) and post-treatment (Monti et al., 1990) significantly and independently predicted relapse following treatment. Flannery et al. (2003) found that craving was a better predictor of consumption during treatment than previous week drinking. However, other researchers have reported that for participants undergoing cue reactivity treatment, craving did not predict alcohol consumption post-treatment (Rohsenow et al., 1994) and that higher craving at the end of treatment actually predicted a longer interval before relapse (Drummond and Glautier, 1994) and less consumption post-discharge (Monti et al., 1993). In reflecting on these conflicting results, some researchers have questioned the ability of craving to predict alcohol consumption and relapse (Drummond et al., 2000; Van den Brink, 1997).

Questionnaires based on differing definitions and theories of craving (e.g., withdrawal-based models, cognitive, psychobiological, motivational) and differences in study methodology (e.g., evaluating craving in participants in standard alcohol treatment versus cue reactivity treatment) may contribute to the mixed findings in the literature (Drummond et al., 2000; Skinner & Aubin, 2010). Further, differential results on craving-consumption relationships may also be due in part to previous reliance on cross-sectional research designs; single time point measures may not be sufficient to elucidate how craving and alcohol consumption relate on a daily basis. Many cross-sectional studies measured craving during alcohol treatment and examined the relationship between a single time point measure and subsequent alcohol use (Bottlender and Soyka, 2004; Drummond and Glautier, 1994; Flannery et al., 2003; Gordon et al., 2006; Monti et al., 1993, 1990; Rohsenow et al., 1994). In this study, we evaluate the relationship between craving and alcohol consumption longitudinally using daily process data.

A limited number of studies have evaluated the craving-alcohol consumption relationship with daily process designs in patients who were participating in or recently completed specialized substance abuse treatment. These studies uniformly found that craving was significantly associated with drinking during treatment (Kavanagh et al., 2009) and relapse (Litt et al., 2000; Oslin et al., 2009). Another study found that craving predicted drinking when participants were prescribed acamprosate or naltrexone therapy to treat alcohol addiction and craving pharmacologically (Richardson et al., 2008).

The current study evaluates the daily relationship between craving and alcohol consumption using an interactive voice response (IVR) telephone system to collect daily craving and drinking reports over 180 days. We use these data to examine the relationship between craving and alcohol consumption while controlling for important confounders. The analyses

Withdrawal models of craving may support a bidirectional relationship. Withdrawal occurs after reduction or cessation in drinking (APA, 1994) and results in reduced glutamatergic and g-aminobutyric acid (GABA)ergic inhibition and increased glutamatergic excitatory neurotransmission which leads to withdrawal symptoms (Tsai et al., 1995). Researchers have theorized that withdrawal can be an unconditioned physiological response to a decrease in drinking and that withdrawal can become a conditioned response elicited by cues in the environment associated with withdrawal or drinking (Wikler, 1965; Siegel, 1998; Drummond et al., 1990). Researchers have hypothesized that craving is part of the withdrawal process and occurs with both unconditioned and conditioned withdrawal (Drummond et al., 2000; Heinz et al., 2003; Ludwig and Wikler, 1974; Shiffman and Jarvik, 1976; Tiffany, 1999; Wikler, 1948). A physiological consequence of heavy drinking may be unconditioned withdrawal craving, and in this manner, drinking may predict future craving. In addition, conditioned environmental stimuli may elicit withdrawal craving and an individual may drink to relieve the craving. In this manner, craving may also predict drinking. Studies examining craving and alcohol consumption have often limited their statistical analyses to unidirectional craving predicting drinking. The current study contributes to the literature in this regard by evaluating a bidirectional craving and alcohol consumption relationship over time using daily process measures.

Another question from the current literature is whether craving and alcohol consumption are significantly correlated beyond a single day or momentary assessment. Many factors, including pharmacological and environmental cues may contribute to across day associations between craving and drinking. First, the DSM-IV TR suggests that withdrawal can occur several hours to a few days after alcohol consumption and evidence from the literature supports this (Foy et al., 1997). In this regard, it would be possible for an individual to drink on one day but not experience unconditioned withdrawal craving until the next day, thus a lagged association might be observed. In addition, although conditioned stimuli in the environment may elicit conditioned withdrawal craving, craving does not necessarily lead to immediate drinking, which has been theorized by Tiffany (1999) and found in daily process studies (Krahn et al., 2005; Litt et al., 2000). Individuals interested in decreasing the frequency of alcohol consumption may attempt to resist or delay drinking in response to craving. Thus, it would be possible for someone to encounter a conditioned stimulus that elicits craving on one day but resist drinking until the following day, and a lagged association may be observed. This may be the case with individuals who have received advice from a physician to decrease their drinking, as participants had in the current study.

The current literature has examined the craving-drinking relationship within a single day (Kavanagh et al., 2009; Richardson et al., 2008) and within multiple time points throughout a day (Litt et al., 2000). To our knowledge, no studies have examined the association between craving and alcohol consumption from one day to the next, although theory suggests that these variables may operate across days. For these reasons, the current study evaluated the relationship between craving and alcohol consumption from day X to day X +1.

Finally, few studies have explored factors that may moderate the craving-drinking relationship. Gender differences may be important to evaluate because gender disparities have been found in biological and social risk factors for alcohol use disorders (AUD's), with men generally being at greater risk for developing AUD's (World Health Organization, 2011). It is possible that gender differences in response to craving may be one factor that

contributes to men being more likely to develop an AUD. Currently, there are inconsistencies in cross-sectional evaluations of gender differences in craving in the literature. Although it is generally agreed that women are more likely to experience craving in response to depression (Rubonis et al., 1994; Zilberman et al., 2007), studies have produced conflicting results in identifying how craving and drinking relate between genders. Studies have found 1) no differences in the association between craving and consumption in men and women (Chakravorty et al., 2010), 2) that craving following drinking is elevated for males only (Willner et al., 1998) and 3) that craving predicted craving/cued relapses in women, but not men (Zywiak et al., 2006). The role of gender in the craving-drinking relationship remains unclear and researchers have called for daily process examination of gender differences in craving and drinking (Krahn et al., 2005; Vukovi et al., 2008) which could help clarify inconsistencies found in cross-sectional literature. Thus the present study also conducted an exploratory analysis of the moderating effect of gender in the craving-drinking relationship.

#### Hypotheses

We hypothesized that there would be a significant bi-directional relationship between craving and drinking, thus that craving on one day would predict next day alcohol consumption, and that total alcohol consumption on one day would predict next day craving intensity.

## **Materials and Methods**

Data for the current manuscript were obtained from a study that evaluated the use of IVR following a brief alcohol intervention in a primary care setting (Helzer et al., 2008). The main objective of the original study was to determine if self-monitoring via IVR with or without feedback would produce improved outcomes compared to no self-monitoring following a brief intervention. Four experimental conditions were compared: no IVR, IVR only, IVR plus monthly feedback, and IVR plus monthly feedback and monetary calling incentive. The feedback groups received monthly mailed graphs that displayed the number of drinks reported on each of the past 30 days juxtaposed with a line representing their drinking goal and a brief note of encouragement from the Principal Investigator.

#### **Participants**

Participants were recruited from April 2000 to July 2003 from 15 primary care offices in the Burlington, VT metropolitan area. Primary care providers screened their patients for heavy alcohol use and, when appropriate, conducted brief alcohol use interventions. Patients who were willing to participate in the randomized trial were referred to the research staff. Participants were included in the study if they reported recent (past 3 month) alcohol consumption beyond NIAAA's guidelines for low risk drinking: 1) average daily or weekly alcohol use of no more than 2 drinks per day/14 per week for men or 1 per day/7 per week for women, or 2) daily maximum of 5 drinks for men or 4 for women (National Institute on Alcohol and Alcohol Abuse (NIAAA), 2005). Both alcohol dependent and non-dependent heavy drinkers were included in the sample to allow for generalizability of study results to other primary care samples. Although the DSM-IV TR considers a categorical dependent/ not diagnosis, excluding non-dependent participants would have removed significant variability in the sample, as a portion of our study sample had symptoms of alcohol dependence but narrowly missed the alcohol dependence diagnostic threshold. Exclusion criteria for the study included current (past year) DSM-IV diagnosis of substance dependence other than alcohol, nicotine, or marijuana, current diagnosis of psychosis, or of major depression with a recent initiation or change in medication. Participants with major

depression who did not have a recent change or initiation in depression medication were included in the study.

#### Demographics

The final study sample included 246 participants (166 men, 80 women) with mean age of 46 years (SD=13, range= 21-82). Ninety-seven percent of participants were Caucasian/non-Hispanic, 76% reported being employed full time, and participants completed a mean of 15 years of education. Sixty-six percent of patients met criteria for alcohol dependence at baseline, as measured by the Composite International Diagnostic Interview-Substance Abuse Module (Cottler et al., 1989).

#### Procedure

Research personnel contacted each referral by telephone to briefly explain the study. Participants were scheduled for an in-person consent and assessment at our research office. Detailed study procedures and the full assessment battery were presented in previous literature (Helzer et al., 2008) and briefly described here. Participants received a 20 minute training session in which they were oriented to using the IVR and instructed on reporting standard drink volumes. Participants were provided a toll-free, 24 hour access phone number to contact the IVR and were asked to call daily for 6 months (180 days). The IVR call was a 2-minute questionnaire that assessed alcohol consumption (number of standard servings of beer, liquor, and wine assessed separately), craving intensity, reasons for drinking/abstaining from drinking, questions about psychological status (stress, happiness, anger, sadness), physical health, relationship with partner, partner alcohol use, and whether the participant was intoxicated at the time of the call. All IVR questions inquired about the previous day to ensure consistent reporting period.

#### **Outcome and Predictor Variables**

This study evaluated the relationship between two time-varying outcome variables assessed on the IVR daily questionnaire: craving rating and total number of alcoholic drinks. Craving was assessed with the following prompt: "Rate your urge to drink yesterday on a scale of 0 to 9, with 0 being no urge to drink and 9 being the strongest urge ever to drink." Measuring craving with a single question has been shown to have test-retest reliability (Cooney et al., 1997) and convergent validity with standard, multi-item measurements (Rosenberg and Mazzola, 2007) and allowed us to maintain brevity in the questionnaire. Other daily process studies have measured craving with a single item (Litt et al., 2000; Richardson et al., 2008) and found craving to be associated with drinking and relapse. In addition, the craving item asked participants to retrospectively rate yesterday's craving, and retrospective recall of past craving has been shown to have predictive validity for alcohol consumption in the standardized assessments such as the Penn Alcohol Craving Scale (Flannery et al., 1999). Total number of drinks was assessed with the following prompt using three separate questions for each type of alcohol: "How many [beers; drinks containing liquor; glasses of wine] did you have yesterday?" Validity of previous day alcohol consumption reported via IVR has previously been demonstrated (Searles et al., 1995). Potential confounding variables with theoretical (Ayer et al., 2011; Chakravorty et al., 2010; Yoon et al., 2006) and statistical relevance to the models included gender, alcohol dependency at baseline, depression medication at baseline, study day (1-180), day of the week (Saturday as the reference), and time-varying psychological variables measured on the IVR (stress, anger, sadness, happiness). In order to run the most parsimonious models, potentially confounding variables, including age that did not significantly confound our outcomes were not included in the final models. The effect of gender was explored as a moderator in separate analyses. As was done in the original study, the IVR plus feedback and the IVR plus feedback and

monetary incentive groups were collapsed for analysis, as the original study found no significant differences in outcome between those two groups (Helzer et al., 2008).

#### Analysis

Descriptive and regression analyses were conducted in SPSS Version 20 (*SPSS*, 2011) utilizing the longitudinal data environment, clustering by unique identification number and sorting by time since beginning of study (study day) consecutively from 1 to 180. SPSS uses pairwise exclusion for cases with missing data. Associations between repeated outcomes and predictors were modeled using the SPSS general linear model environment with generalized estimating equations (GEE) (Hardin and Hilbe, 2003). For longitudinal analysis, reports from the same individual over time will be correlated compared to reports between subjects (Hardin and Hilbe, 2003). GEE analysis was chosen because this analytic technique accounts for this within-subject report correlation. We explored several potential within-ID correlation structures (exchangeable, unstructured, autoregressive) and determined that an exchangeable correlation structure fit the data best based on the Quasi-Likelihood under the Independence Model Criterion(QIC) (Pan, 2001). Therefore, all GEE models assumed an exchangeable correlation structure.

First, a GEE model was run to determine the association between craving rating and total number of drinks the next day, controlling for all potential confounders listed previously. Next, the GEE model was reversed to examine whether total number of drinks was associated with next day craving rating, controlling for all confounders listed previously. Finally, the potential moderating effect of gender was explored by including an interaction between gender and craving rating to the GEE models. (In the moderating analysis, gender was not also evaluated as a confounder in the same analysis.) A significant interaction term (p<0.05) was explored by stratifying the GEE model across levels of gender.

In addition to these analyses, the association between same day craving and alcohol consumption while controlling for the same confounders were also evaluated using GEE. This was not our main research question, and we cannot determine direction of association between craving and alcohol consumption. However, we provided results of these analyses as evidence for the validity of our craving assessment and to provide data for comparison to other research reports in the literature.

#### Results

Participants completed a median of 91% of calls (interquartile range 32% to 100%) over the 180 study days (Helzer et al., 2008). Rather than calling intermittently, participants tended to call regularly for various points in time until they discontinued calling. Participants completed a total of 27,178 IVR reports.

Descriptive statistics were run to examine the occurrence of craving and the quantity and frequency of alcohol consumed during the study. Every participant reported experiencing craving at some point during the study. Craving was reported in 89% of the daily reports, and the mean craving rating across the study was 3.5 (standard deviation; SD =.3) on a scale of 0-9. Mean craving rating by day ranged from 3.1 to 4.3 (SD = 2.2 to 2.3). Craving was rated a 6 or higher in 21% of the reports. Participants drank on 75% of study days, and the mean number of drinks per drinking day across the study was 5.0 (SD = 2.5, Range 1-17.5). Mean total drinks by day ranged from 4.0 to 6.5, (SD= 2.8 to 4.3). Patients reported craving on more days than they reported drinking.

In our first GEE model which evaluated the relationship between craving and next day total number of drinks consumed, a one point increase in craving rating was significantly

associated with an increase in average total number of drinks the next day after controlling for confounders, as hypothesized (Table 1). In the second GEE model which examined whether total drinks was associated with next day craving, a one drink increase in total drinks was significantly associated with an increase in next day craving rating after controlling for confounders, as expected (Table 2). In our exploration of whether gender moderated the relationship between craving and total drinks, we found that gender significantly moderated the craving-drinking association (p < .002), so this interaction was further explored by examining the relation between craving and next day drinking within each gender separately. A one point higher increase in craving rating was associated with a larger average increase in the next day total drinks for males than females (Table 3). When reversing the association we found that gender did not significantly moderate this relationship between total drinks and next day craving (p's >.05).

Same-day craving rating and alcohol consumption were strongly correlated, with higher craving being significantly associated with higher alcohol consumption (b=.85, p<.001, 95% CI .75 to .95).

## Discussion

Our findings confirmed our hypothesis and provide evidence that craving ratings on one day were significantly associated with next day total number of drinks consumed, and vice versa. These data suggest there is a dynamic relationship between craving and drinking across days. The bidirectional relationship observed may have resulted from a combination of physiological and conditioned withdrawal craving. Heavy drinkers may experience withdrawal symptoms, including withdrawal craving, following an episode of drinking (Drummond et al., 2000; Ludwig and Wikler, 1974) and individuals may be particularly likely to experience withdrawal if they are attempting to decrease the frequency of their drinking. Participants in the current study were advised by a physician to decrease their alcohol use, so they may have attempted to do so. In this manner, drinking may have influenced subsequent withdrawal craving for participants in our sample. Conditioned withdrawal craving may have contributed to craving predicting next day alcohol consumption in our sample. Heavy drinkers may experience conditioned withdrawal craving cued by environmental stimuli associated with alcohol consumption or withdrawal (Drummond et al., 2000; Ludwig and Wikler, 1974). Conditioned withdrawal craving may influence an individual to drink alcohol to relieve the craving, however individuals attempting to decrease drinking frequency may attempt to delay drinking. This may result in a lagged craving-drinking relationship, as was observed in our sample. In this manner, both unconditioned physiological and conditioned withdrawal craving may have contributed to the bidirectional, across-day association between craving and drinking observed in the study.

In addition to our main findings, descriptive analyses revealed that participants reported craving in most (89%) IVR reports during the 6 month study period, and that all participants reported craving at some point in the study. Our findings confirm theoretical and clinical assumptions that craving is a frequent problem for heavy drinkers (Addolorato et al., 2005; de Bruijn et al., 2004). The findings are in contrast to daily process studies that used ecological momentary assessment (EMA) and found low instances of craving in participants in substance abuse treatment or recently completed treatment (Cooney et al., 2007; Krahn et al., 2005; Litt et al., 2000). However, a direct comparison between our findings and previous literature is not possible. Our study measured craving once per day and the EMA studies reported percent of craving instances measured multiple times per day. It is possible that we observed very high rates of craving in our sample because we evaluated heavy drinkers, 66% of whom met criteria for alcohol dependence, and who were seldom engaged in or recently discharged from specialized treatment for alcoholism. It is also possible that, in our

sample, craving rates were high following a brief intervention, if patients were attempting to cut down on drinking. Tiffany (1990) theorized that individuals dependent on alcohol who are attempting to maintain abstinence may experience urges to drink, and our findings may be in accordance with this possibility. Future research is needed to examine how craving operates in different contexts.

In reference to potential moderating effects, exploration of gender effects revealed gender differences in the craving-drinking relationship. This relationship was stronger in males than in females and it is possible that a differential response to craving may be one factor that contributes to males having a higher prevalence of AUD's. Our results suggest that males may especially benefit from interventions focused on craving reduction. To our knowledge, no studies have evaluated whether males and females respond differentially to alcohol treatment with a focus on craving compared to without, although future research on this topic may be warranted.

Several limitations of the study are important to mention. First, all data were collected via self-report. While it is possible that participants underreported alcohol use, this seems unlikely because the high level of candor and validity of IVR reports of alcohol consumption have been demonstrated previously (Kobak et al., 1997; Searles et al., 1995). Second, ratings of daily craving and drinking were reported retrospectively for the previous day. It is possible that in reporting both variables for the previous day, participants' ratings of craving may have been inflated or attenuated by how much they reported drinking. An improvement in this methodology for future studies would be to use ecological momentary assessment to collect reports as craving occurs in the moment. This would decrease simultaneous reporting of both craving and alcohol consumption if the two did not occur at the same time. Third, craving was measured from a single question with a ten-point scale. This is a necessary sacrifice as conciseness is needed to maintain the high call compliance necessary for robust daily process data. Investigators have demonstrated that single item craving scales have test-retest reliability (Cooney et al., 1997) and convergent validity with standard, multi-item measurements (Rosenberg and Mazzola, 2007). However, daily process multi-item craving scales could further elucidate nuances in the craving-drinking relationship. Finally, it is likely that other variables not measured in this study may play an important role in the relationship between craving and drinking. Examples might include personality factors and family history of addiction. Investigating these and other theoretical confounders using daily process methods could further decipher the relationship between craving and drinking, and might provide further insight into the etiology of alcohol use disorders and/or suggest new approaches to intervention.

#### Implications

Data from the current daily assessment of a large sample of heavy drinkers over a 6 month period suggest a significant across-day, bi-directional relationship between craving and drinking may be a key factor contributing to heavy drinking. Future research evaluating a potential cyclical relationship between craving and drinking may be warranted, and may further elucidate potential mechanisms that maintain problem drinking. In addition, we found that craving occurs frequently following a brief intervention by a primary care physician. This finding may be representative of craving in heavy drinkers seldom in specialized substance abuse treatment, or craving in response to advice to decrease drinking. Results should generalize to other primary care settings in which participants receive brief interventions. However interpretations should be made with caution about generalizability to participants in specialized alcohol treatment programs. Further daily process research is needed to decipher how craving operates in these different contexts.

NIAAA guidelines do not specifically recommend that primary care physicians evaluate craving during brief interventions. Based on our findings, we recommend that physicians discuss craving symptomatology along with alcohol consumption during brief interventions and at follow up, particularly with male patients. Physician-delivered advice regarding the craving-alcohol consumption relationship and suggestions on how to cope with it might increase the efficacy of brief intervention in primary care settings.

### Acknowledgments

Funded by the National Institute on Alcohol Abuse and Alcoholism (R01-AA11954)

#### References

- Addolorato G, Leggio L, Abenavoli L, Gasbarrini G. Neurobiochemical and clinical aspects of craving in alcohol addiction: A review. Addictive Behaviors. 2005; 30:1209–1224. [PubMed: 15925129]
- APA. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. American Psychiatric Association; Washington DC: 1994.
- Ayer LA, Harder VS, Rose GL, Helzer JE. Drinking and stress: an examination of sex and stressor differences using IVR-based daily data. Drug Alcohol Depend. 2011; 115:205–212. [PubMed: 21146940]
- Bottlender M, Soyka M. Impact of craving on alcohol relapse during and 12 months following outpatient treatment. Alcohol and Alcoholism. 2004; 39:357–361. [PubMed: 15208171]
- Chakravorty S, Kuna ST, Zaharakis N, O'Brien CP, Kampman KM, Oslin D. Covariates of craving in actively drinking alcoholics. Am J Addict. 2010; 19:450–457. [PubMed: 20716308]
- Cooney NL, Litt MD, Cooney JL, Pilkey DT, Steinberg HR, Oncken CA. Alcohol and Tobacco Cessation in Alcohol-Dependent Smokers: Analysis of Real-Time Reports. Marlatt, G. Alan, Witkiewitz, Katie. 2007; 21:277–286.
- Cooney NL, Litt MD, Morse PA, Bauer LO, Gaupp L. Alcohol cue reactivity, negative-mood reactivity, and relapse in treated alcoholic men. Journal of Abnormal Psychology. 1997; 106:243– 250. [PubMed: 9131844]
- Cottler LB, Robins LN, Helzer JE. The Reliability of the CIDI-SAM: A Comprehensive Substance Abuse Interview. British Journal of Addiction. 1989; 84:801–814. [PubMed: 2758153]
- De Bruijn C, Korzec A, Koerselman F, Van Den Brink W. Craving and withdrawal as core symptoms of alcohol dependence. Journal of Nervous and Mental Disease. 2004; 192:494–502. [PubMed: 15232320]
- Drummond DC, Cooper T, Glautier SP. Conditioned learning in alcohol dependence: implications for cue exposure treatment. Br J Addict. 1990; 85:725–743. [PubMed: 2198966]
- Drummond DC, Glautier S. A controlled trial of cue exposure treatment in alcohol dependence. Journal of Consulting and Clinical Psychology. 1994; 62:809–817. [PubMed: 7962885]
- Drummond DC, Litten RZ, Lowman C, Hunt WA. Craving Research: Future Directions. Addiction. 2000; 95:S247–S255. [PubMed: 11002919]
- Flannery BA, Poole SA, Gallop RJ, Volpicelli JR. Alcohol craving predicts drinking during treatment: An analysis of three assessment instruments. Journal of Studies on Alcohol. 2003; 64:120–126. [PubMed: 12608492]
- Flannery BA, Volpicelli JR, Pettinati HM. Psychometric Properties of the Penn Alcohol Craving Scale. Alcoholism: Clinical and Experimental Research. 1999; 23:1289–1295.
- Foy A, Kay J, Taylor A. The course of alcohol withdrawal in a general hospital. QJM. 1997; 90:253–261. [PubMed: 9307759]
- Gordon SM, Sterling R, Siatkowski C, Raively K, Weinstein S, Hill PC. Inpatient Desire to Drink as a Predictor of Relapse to Alcohol Use Following Treatment. The American Journal on Addictions. 2006; 15:242–245. [PubMed: 16923671]
- Hardin, JW.; Hilbe, J. Generalized Estimating Equations. CRC Press; 2003.

- Heinz A, Lober S, Georgi A, Wrase J, Hermann D, Rey E-R, Wellek S, Mann K. REWARD CRAVING AND WITHDRAWAL RELIEF CRAVING: ASSESSMENT OF DIFFERENT MOTIVATIONAL PATHWAYS TO ALCOHOL INTAKE. Alcohol and Alcoholism. 2003; 38:35–39. [PubMed: 12554605]
- Helzer JE, Rose GL, Badger GJ, Searles JS, Thomas CS, Lindberg SA, Guth S. Using interactive voice response to enhance brief alcohol intervention in primary care settings. Journal of Studies on Alcohol and Drugs. 2008; 69:251–258. [PubMed: 18299766]
- Jones KD, Gill C, Ray S. Review of the Proposed DSM-5 Substance Use Disorder. Journal of Addictions & Offender Counseling. 2012; 33:115–123.
- Kavanagh DJ, May J, Andrade J. Tests of the Elaborated Intrusion Theory of Craving and Desire: Features of Alcohol Craving During Treatment for an Alcohol Disorder. British Journal of Clinical Psychology. 2009; 48:241–254. [PubMed: 19364447]
- Kobak KA, Taylor L. vH, Dottl SL, Greist JH, Jefferson JW, Burroughs D, Katzelnick DJ, Mandell M. Computerized Screening for Psychiatric Disorders in an Outpatient Community Mental Health Clinic. Psychiatric Services. 1997; 48:1048–1057. [PubMed: 9255838]
- Krahn DD, Bohn MJ, Henk HJ, Grossman JL, Gosnell B. Patterns of Urges During Early Abstinence in Alcohol-Dependent Subjects. The American Journal on Addictions. 2005; 14:248–255. [PubMed: 16019975]
- Litt MD, Cooney NL, Morse P. Reactivity to alcohol-related stimuli in the laboratory and in the field: predictors of craving in treated alcoholics. Addiction. 2000; 95:889–900. [PubMed: 10946438]
- Loeber S, Croissant B, Heinz A, Mann K, Flor H. Cue exposure in the treatment of alcohol dependence: Effects on drinking outcome, craving and self-efficacy. British Journal of Clinical Psychology. 2006; 45:515–529. [PubMed: 17076961]
- Ludwig AM, Wikler A. "Craving" and relapse to drink. Quarterly Journal of Studies on Alcohol. 1974; 35:108–130.
- Monti PM, Abrams DB, Binkoff JA, Zwick WR. Communication skills training, communication skills training with family and cognitive behavioral mood management training for alcoholics. Journal of Studies on Alcohol. 1990; 51:263–270. [PubMed: 2342366]
- Monti PM, Rohsenow DJ, Rubonis AV, Niaura RS, Sirota AD, Colby SM, Goddard P, Abrams DB. Cue exposure with coping skills treatment for male alcoholics: A preliminary investigation. Journal of Consulting and Clinical Psychology. 1993; 61:1011–1019. [PubMed: 7906700]
- National Institute of Alcohol and Alcohol Abuse. Helping Patients With Alcohol Problems: A Clinician's Guide (No. 05–3769). NIH: the Institute; Bethesda, MD: 2005.
- Oslin DW, Cary M, Slaymaker V, Colleran C, Blow FC. Daily ratings measures of alcohol craving during an inpatient stay define subtypes of alcohol addiction that predict subsequent risk for resumption of drinking. Drug and Alcohol Dependence. 2009; 103:131–136. [PubMed: 19443131]
- Pan W. Akaike's information criterion in generalized estimating equations. Biometrics. 2001; 57:120– 125. [PubMed: 11252586]
- Richardson K, Baillie A, Reid S, Morley K, Teesson M, Sannibale C, Weltman M, Haber P. Do acamprosate or naltrexone have an effect on daily drinking by reducing craving for alcohol? Addiction. 2008; 103:953–959. [PubMed: 18482418]
- Rohsenow DJ, Monti PM, Rubonis AV, Sirota AD, Niaura RS, Colby SM, Wunschel SM, Abrams DB. Cue reactivity as a predictor of drinking among male alcoholics. Journal of Consulting and Clinical Psychology. 1994; 62:620–626. [PubMed: 8063989]
- Rosenberg H, Mazzola J. Relationships Among Self-Report Assessments of Craving in Binge-Drinking University Students. Addictive Behaviors. 2007; 32:2811–2818. [PubMed: 17524566]
- Rubonis AV, Colby SM, Monti PM, Rohsenow DJ. Alcohol cue reactivity and mood induction in male and female alcoholics. Journal of Studies on Alcohol. 1994; 55:487–494. [PubMed: 7934057]
- Searles JS, Perrine MW, Mundt JC, Helzer JE. Self-Report of Drinking Using Touch-Tone Telephone: Extending the Limits of Reliable Daily Contact. Journal of Studies on Alcohol and Drugs. 1995; 56:375.
- Shiffman SM, Jarvik ME. Smoking withdrawal symptoms in two weeks of abstinence. Psychopharmacology. 1976; 50:35–39. [PubMed: 827760]

- Siegel, S. Drug anticipation and drug tolerance. In: Lader, M., editor. Psychopharmacology of Addiction. Oxford University Press; 1988.
- Skinner MD, Aubin H-J. Craving's place in addiction theory: Contributions of the major models. Neuroscience & Biobehavioral Reviews. 2010; 34:606–623. [PubMed: 19961872]
- SPSS. IBM Corporation; Chicago, IL: 2011.
- Tiffany ST. A cognitive model of drug urges and drug-use behavior: role of automatic and nonautomatic processes. Psychol Rev. 1990; 97:147–168. [PubMed: 2186423]
- Tiffany ST. Cognitive concepts of craving. Alcohol Res Health. 1999; 23:215–224. [PubMed: 10890817]
- Tsai G, Gastfriend DR, Coyle JT. The glutamatergic basis of human alcoholism. The American Journal of Psychiatry. 1995; 152:332–340. [PubMed: 7864257]
- Van den Brink W. Editorial: Craving and Relapse Prevention. European Addiction Research. 1997; 3:107–109.
- Vukovi O, Cveti T, Zebi M, Mari N, Britvi D, Aleksandar Damjanovi , Jašovi -Gaši M. Contemporary Framework for Alcohol Craving. Psychiatria Danubina. 2008; 20:500–507. [PubMed: 19011591]
- Wikler A. Recent progress in research on the neurophysiologic basis of morphine addiction. The American Journal of Psychiatry. 1948; 105:329–338. [PubMed: 18890902]
- Wikler, A. Conditioning factors in opiate addiction and relapse. In: Wiher, DL.; Kassebaum, G., editors. Narcotics. McGraw-Hill; 1965.
- Willner P, Field M, Pitts K, Reeve G. Mood, cue and gender influences on motivation, craving and liking for alcohol in recreational drinkers. Behavioural Pharmacology. 1998; 9:631–642. [PubMed: 9862088]
- World Health Organization. Global Status Report on Alcohol and Health. 2011
- Yoon G, Kim SW, Thuras P, Grant JE, Westermeyer J. Alcohol Craving in Outpatients with Alcohol Dependence: Rate and Clinical Correlates. Journal of Studies on Alcohol. 2006; 67:770–777. [PubMed: 16847547]
- Zilberman ML, Tavares H, Hodgins DC, el-Guebaly N. The Impact of Gender, Depression, and Personality on Craving. Journal of Addictive Diseases. 2007; 26:79–84. [PubMed: 17439871]
- Zywiak WH, Stout RL, Trefry WB, Glasser I, Connors GJ, Maisto SA, Westerberg VS. Alcohol relapse repetition, gender, and predictive validity. J Subst Abuse Treat. 2006; 30:349–353. [PubMed: 16716850]

#### Table 1

Main effect of craving on next day total drinks.

	DV: Next day total drinks					
	b	SE	р	95%CI (low,		
high)						
Craving	.15	.02	.0005	.10,	.19	
Gender <sup>a</sup>	.89	.29	.002	.32,	1.46	
Alcohol dependency (yes/no)	.55	.30	.06		1.22,	
3.44						
Depression medication (yes/no)	-1.33	.31	.0005	-1.93,	72	
Daily stress	.00	.02	.99	04,	.39	
Daily sadness	.01	.02	.49		03	
.05						
Daily anger	.09	.02	.0005	.05,	.13	
Daily happiness	.10	.02	.0005	.06,	.15	
Study day	01	.01	.0005	01,	01	
Day of the week <sup><math>b</math></sup>						
Monday	86	.11	.0005	-1.08,	64	
Tuesday	74	.10	.0005	94,	54	
Wednesday	51	.10	.0005	72,	31	
Thursday	44	.12	.0005	67,	21	
Friday	.31	.13	.02	.04,	.57	
Saturday	.59	.11	.0005	.37,	.82	

Note. DV: dependent variable; b: unstandardized regression coefficient; SE: standard error; p: p-value; CI: confidence interval.

<sup>a</sup>Female is reference category.

<sup>b</sup>Sunday is reference day.

#### Table 2

Main effect of total drinks on next day craving.

	DV: Next day total drinks					
	b	SE	р	95%CI (low		
high)						
Total drinks	.02	.01	.02	.01,	.04	
Gender <sup>a</sup>	.16	.21	.43	26,	.58	
Alcohol dependency (yes/no)	.73	.20	.0005		.34,	
1.13						
Depression medication (yes/no)	.48	.30	.12	12,	1.08	
Daily stress	.10	.01	.0005	.07,	.12	
Daily sadness	.04	.02	.01		.01,	
.07						
Daily anger	.07	.02	.0005	.04,	.10	
Daily happiness	.04	.02	.01	.01,	.08	
Study day	01	.01	.001	01,	01	
Day of the week <sup><math>b</math></sup>						
Monday	27	.05	.0005	37,	17	
Tuesday	20	.05	.0005	30,	11	
Wednesday	10	.05	.03	20,	01	
Thursday	04	.06	.48	15,	.07	
Friday	.25	.06	.0005	.13,	.37	
Saturday	.23	.05	.0005	.14,	.32	

Note. DV: dependent variable; b: unstandardized regression coefficient; SE: standard error; p: p-value; CI: confidence interval.

<sup>a</sup>Female is reference category.

<sup>b</sup>Sunday is reference day.

#### Table 3

Craving predicting next day total drinks stratified by gender.

	DV: Next day total drinks					
	b	SE	р	95%CI (low,		
high)						
Males only						
Craving	.19	.03	.0005	.12,		
.25						
Females only						
Craving	.08	.03	.006	.02,		
.13						

*Note*. DV: dependent variable; *b*: unstandardized regression coefficient; SE: standard error; *p*: *p*-value; CI: confidence interval. Confounders controlled for in the models: gender, alcohol dependency at baseline, depression medication at baseline, study day (1-180), day of the week (Sunday as the reference), and time-varying psychological variables measured on the IVR (stress, anger, sadness, happiness).