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Childhood maltreatment, stressful life events, and alcohol craving in adult drinkers

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Abstract

Background—Little is known about the relationship of stressful life events and alcohol craving in the general population, and whether a history of childhood maltreatment sensitizes individuals to crave alcohol after adult stressors.

Methods—Participants were 22,147 past-year drinkers from Wave 2 (2004–2006) of the National Epidemiologic Survey on Alcohol and Related Conditions. A structured, face-to-face interview assessed past-year stressful life events, alcohol craving, and history of childhood maltreatment. Logistic regression was used to generate adjusted odds ratios (aOR) to evaluate the relationship between stressful life events and craving, adjusting for demographic characteristics and parental history of alcoholism. Interaction between stressful life events and childhood maltreatment was also assessed.

Results—Compared to participants with no stressful life events, those with 3 events had increased odds of moderate alcohol craving (aOR=3.15 [95% CI=2.30–4.33]) and severe craving (aOR=8.47 [95% CI=4.78–15.01]). Stressful life events and childhood maltreatment interacted in predicting severe craving ($p=0.017$); those with 3 events were at higher risk for craving if they had been exposed to childhood maltreatment.

Conclusion—A direct relationship between stressful life events and risk for alcohol craving was observed. Further, history of childhood maltreatment increased the salience of stressful life events

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in adulthood. Future studies should examine the role of psychiatric comorbidity in more complex models of stress sensitization and alcohol craving.

Keywords

alcohol craving; stressful life events; childhood maltreatment; stress sensitivity

INTRODUCTION

In recent years, alcohol craving has gained importance in alcohol research for several reasons, including the association between craving and poor course in both treated alcoholics (Breese et al., 2005, Fox et al., 2007, Sinha et al., 2009, Pilowsky et al., 2013, Higley et al., 2011) and in the general population (de Bruijn et al., 2005). Further, the inclusion of craving as a new criterion for Substance Use Disorders in the DSM-5 (American Psychiatric Association, 2013) has drawn interest to the need to gain a better understanding of craving (Agrawal et al., 2011). This includes elucidating the risk factors for alcohol craving, which can inform efforts aimed at the prevention and treatment of alcohol use disorders (Anton, 1999).

Stress has been a widely investigated risk factor for alcohol craving (Sinha, 2001) in clinical samples (Fox et al., 2007, Higley et al., 2011, Sinha et al., 2009). However, only a small proportion of individuals with a lifetime history of alcohol use disorders typically receive treatment (Cohen et al., 2007, Hasin, 2013). Thus, understanding the factors underlying stress-induced craving outside of a clinical context may provide valuable insight for the development of public health prevention and treatment strategies. In the general population, stressful life events are associated with heavy alcohol consumption (San José et al., 2000, Dawson et al., 2005, Young-Wolff et al., 2012) and with relapse among formerly alcohol dependent adults (Pilowsky et al., 2013). However, whether stressful life events similarly increase the risk for alcohol craving in the general population remains unclear.

Investigation of the relationship between stressful life events and craving should incorporate factors that underlie variation in individual sensitivity to stress (Sinha, 2007). The stress sensitization model (Keyes et al., 2011a) posits that the relationship of adult stressors to adverse health outcomes is determined, in part, by earlier exposure to childhood maltreatment and adversity (Sinha, 2007, Hyman et al., 2007, Harkness et al., 2006, Keyes et al., 2012). Three studies have supported the stress sensitization model for alcohol outcomes. In a U.S. twin sample (Young-Wolff et al., 2012), stressful life events were associated with heavier drinking among women exposed to childhood maltreatment than among those without such exposure. In a sample of Israeli adults, the risk for current alcohol use disorders was increased among those exposed to wartime stressors, but only among those with a history of childhood maltreatment (Keyes et al., 2014). In a predominantly African American community sample in Detroit, childhood maltreatment and neighborhood physical disorder were found to interact in predicting incident binge drinking (Keyes et al., 2012). Determining if the stress sensitization model similarly holds for alcohol craving would provide novel evidence about an important element in vulnerability to alcohol outcomes.

Therefore, this study addressed two primary questions. (1) What is the association between past-year stressful life events and alcohol craving among adult current drinkers in the general population? (2) Does a history of childhood maltreatment modify the relationship between past-year stressful life events and alcohol craving? In addition, given the high degree of psychiatric comorbidity in the general population (Krueger, 1999, Hasin et al., 2007), we explored whether incorporating internalizing and externalizing disorders into the analysis suggested the potential for more complex models. Psychological distress (an internalizing condition) may interfere with managing stressful life events (Sinha and Li, 2007) and also influence craving (Sinha, 2007). Externalizing disorders may represent more general underlying vulnerability to substance disorder phenotypes (Hicks et al., 2004, Kendler et al., 2003). The research was conducted in a large national sample.

METHODS

Sample

Participants were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a representative sample of the civilian, non-institutionalized adult population of the United States, including individuals living in households, military personnel living off base, and people residing in select group quarters (Grant et al., 2004b). The NESARC oversampled African Americans, Hispanics, and young adults aged 18-24, with one adult selected for interview per household. The survey was conducted in two waves: Wave 1, conducted in 2001-2002, and Wave 2, conducted in 2004-2005. Wave 2 included 34,653 of the original respondents, for a cumulative total response rate at Wave 2 of 70.2% (Grant et al., 2009). We analyzed data from Wave 2 because the alcohol craving and childhood maltreatment items were assessed in this wave. Of the Wave 2 respondents, 63.9% (n=22,147) were current drinkers (at least one drink in the past year) and were included in our analysis.

Measures

Outcome: Alcohol Craving—Alcohol craving was assessed with two separate measures. Moderate alcohol craving was indicated by a positive response to the question “In the past year, have you felt a very strong desire to drink?” Severe craving was indicated by a positive response to the question “In the past year, have you ever wanted a drink so badly that you couldn’t think of anything else?” These questions were designed to measure the craving criterion in DSM-5 (American Psychiatric Association, 2013, Hasin et al., 2013). These or very similar items have been used in previous studies, including genetic studies (Ehlers et al., 2010, Peer et al., 2013), and the National Longitudinal Alcohol Epidemiologic Survey (Grant et al., 2004a, Compton et al., 2004). A general population reliability study of alcohol dependence with similar craving measures also showed excellent test-retest reliability (Grant et al., 1995).

Past-Year Stressful Life Experiences—Of the fourteen binary stressful life events in the past year measured at Wave 2, six were selected for this study based on their known associations with increased risk of psychopathology (Mazure, 1998, McLaughlin, 2010) and heavy alcohol consumption (Dawson et al., 2005). These included: (1) “Were you fired or

laid off from a job?” (2) “Were you unemployed and looking for a job longer than a month?” (3) “Did you get separated, divorced, or break off a steady relationship?” (4) “Have you experienced major financial crisis, declared bankruptcy, or more than once been unable to pay bills on time?” (5) “Did you have serious trouble with the police or the law?” and (6) “Any family members or close friends died?” Recent NESARC studies of stressful life events and alcohol relapse used similar measures (Pilowsky et al., 2013). The six responses were combined into a categorical variable representing experience of none, one to two, or three or more stressful events, consistent with previous research in the NESARC (McLaughlin, 2010).

Childhood maltreatment—The childhood maltreatment measure is described elsewhere (Ruan et al., 2008). In brief, it includes 19 items assessing five types of childhood maltreatment, adapted from the Conflict Tactics Scale (CTS) and the Childhood Trauma Questionnaire (CTQ), two empirically validated scales (Bernstein et al., 1994, Straus, 1990). Respondents were asked about events occurring prior to age 18, and response options ranged from never (1) to very often or always (5). Respondents were considered positive for *physical abuse* (18.5% of the sample) if they reported that a parent/caregiver had at least “sometimes” physically harmed or injured them. Respondents were considered positive for *emotional abuse* (8.1%) if they reported that a parent/caregiver had verbally abused, threatened, or made them fearful of violence at least “fairly often”. *Sexual abuse* (10.5%) was considered positive if respondents had any sexual contact with an adult that was unwanted, or that occurred before the respondent was old enough to understand what was happening. The five emotional neglect items asked respondents if their family encouraged their success, made them feel special, was a source of strength and support, believed in them, or if the family was close-knit. These items were reverse coded (“never” having a value of 5) and tallied, with a score of at least fifteen indicating *emotional neglect* (8.5%). These thresholds are similar to those utilized in previous research (Dube et al., 2003, Dong et al., 2003, Afifi et al., 2011). For *physical neglect* (7.3%), respondents were considered positive if they reported at least “fairly often” that a parent/caregiver made them do age-inappropriate chores, left them unsupervised before age 10, or did not provide them with basic materials, sustenance, or care. While previous studies have used a threshold of answering “sometimes” to any one of these items (Afifi et al., 2011, Fenton et al., 2013, Waxman et al., 2013) we set the threshold at “fairly often” to maintain a consistent level of severity (prevalence) across the five maltreatment types. The items underlying these maltreatment types have shown excellent intraclass test-retest reliability, with coefficients ranging from 0.79 for physical abuse to 0.88 for emotional abuse (Ruan et al., 2008). To facilitate interpretation, a binary variable was created indicating experiencing at least one type of childhood maltreatment (31.1%).

Other covariates—All models controlled for gender, age (18-29, 30-33, 45-64, >65), race/ethnicity (white, black, Hispanic, other), education (less than high school, high school/G.E.D., some college, advanced degree) and parental history of alcoholism (biological father or mother ever an alcoholic or problem drinker), an AUDADIS measure with excellent test-retest reliability (Dawson and Grant, 1998).

Psychiatric comorbidity—To explore whether more complex models might be operating in the relationship between stress sensitization and alcohol craving, we used variables representing internalizing and externalizing disorders (Krueger, 1999). Internalizing disorders were represented with a variable indicating past-year mood or anxiety disorders, including major depression, dysthymia, panic disorder, social phobia, specific phobia, or generalized anxiety, consistent with prior work on alcohol and life events (Dawson et al., 2005). Externalizing comorbidity was defined with variables indicating lifetime antisocial personality disorder and past-year drug dependence (marijuana, cocaine, opioids, amphetamines, sedatives, tranquilizers, hallucinogens, inhalants, heroin, and other drugs) at Wave 2. Alcohol dependence was not included as an externalizing disorder because it was highly collinear with parental history of alcoholism, and is also highly collinear with craving (Agrawal et al., 2011, Keyes et al., 2011b), the main outcome of the present study. Test-retest reliability for internalizing and externalizing disorders is fair to excellent (Grant et al., 2003).

Analysis

Weighted cross-tabulations were used to provide prevalence estimates and standard errors for alcohol craving and its relationship to socio-demographic characteristics and the primary study predictors (stressful life events, childhood maltreatment). Bivariate associations between craving and each primary predictor were tested with Pearson's chi-square. Multivariable logistic regression was used to obtain adjusted odds ratios (aOR) for past-year alcohol craving at each level of stressful events (no events, one or two events, or at least three events), with no events as the reference category. Statistical interaction was evaluated to determine whether the association between stressful life events and alcohol craving differed between individuals with and without a history of childhood maltreatment. Interaction effects were assessed on the additive scale, now the preferred method to test for interactions in epidemiology (Andersson et al., 2005, Knol et al., 2011, Kalilani and Atashili, 2006). Interaction was assessed by back-transforming the parameters from a logistic regression model (which included stressful life events, childhood maltreatment, their interaction, and additional covariates) to the probability scale. These probabilities (prevalence) are used to separately estimate the risk difference (RD) at one or two and at least three stressful life events compared to no events, for individuals with and without childhood maltreatment. The estimate for the interaction term represents the interaction contrast (IC), or the "difference in risk differences" between those with and without childhood maltreatment. Adjusted and unadjusted ICs were calculated through the PRED_EFF command in SUDAAN, which uses sample weights to compute marginally predicted risk differences (Research Triangle Institute, 1989). Wald-type t-tests were used to test if the IC was significantly ($p < 0.05$) greater than zero, indicating that prior history of childhood maltreatment differentially influenced the risk for alcohol craving at the level of stressful events experienced.

In our primary analyses of main effects and interactions, we included demographics and parental history of alcoholism in the models (Model A). In our exploratory models of main effects and interactions, we added internalizing disorders (Model B), externalizing disorders (Model C) and internalizing plus externalizing disorders (Model D).

RESULTS

The prevalence of moderate alcohol craving among the 22,147 past-year drinkers was 3.41% (n=741), and the prevalence of severe alcohol craving was 0.84% (n=183). The prevalence of both craving measures differed significantly by gender (higher in males), age (higher in those under 30), educational attainment (higher in those with less than a high school degree), parental history of alcoholism, past-year internalizing disorders and the externalizing disorders (lifetime history of antisocial personality disorder and past-year drug dependence (Table 1).

No past-year stressful life events were reported by 52.8% of the sample, 42.3% reported one to two events, and 4.9% reported three or more events (Table 2). While sex was not associated with the number of stressful life events, younger age, non-White ethnicity, lower educational attainment, parental history of alcoholism, and internalizing and externalizing disorders were associated with reporting more stressful life events. Further, history of childhood maltreatment was associated with past-year stressful life events ($p<0.001$). Among individuals with such a history, 45.9%, 46.5%, and 7.6% reported no events, one to two events, and three or more events, respectively, while among individuals without such a history, 56.0%, 40.4%, and 3.6% reported no events, one to two events, and three or more events, respectively.

A direct relationship between the number of events and the risk of alcohol craving was observed (Table 3). Among individuals with no stressful life events, the prevalence of moderate and severe craving was 2.41% and 0.33%, respectively. The prevalence of moderate and severe craving rose as the number of stressful events increased, from 3.96% and 1.02% among respondents who experienced one or two events, to 9.56% and 4.90% among respondents who experienced three or more events, respectively.

The risk of moderate alcohol craving was significantly elevated among participants who experienced stressful life events compared to those who experienced no stressful life events (Model A): one or two stressful events: aOR=1.53; 95% CI 1.24-1.90; three or more stressful events: aOR=3.15; 95% CI 2.30-4.33; Table 3). A significantly elevated risk of severe alcohol craving was also shown among participants who experienced stressful life events compared to those who experienced no stressful life events (Model A): aOR=2.54; 95% CI 1.58-4.08 and aOR=8.47; 95% CI 4.78-15.01, respectively.

The relationship between stressful life events and the prevalence of severe alcohol craving was modified by a history of childhood maltreatment (stress sensitization; Table 4). In Model A, the risk difference for at least three stressful events compared to no events was significantly greater among those with a prior history of maltreatment (RD: 4.6%, $p<0.001$) than among individuals without a prior history of maltreatment (RD: 1.7%, $p=0.005$; IC: 2.8%, $p=0.017$).

In the exploratory analyses, main effects of stressful life events and childhood maltreatment on moderate and severe craving remained significant after adding internalizing and externalizing comorbidity (Models B, C and D). Adding the internalizing variable to the interaction model for severe craving (Model B) resulted in an IC of 1.6%, $p=.07$. Adding the

externalizing variable (Model C) resulted in an IC of 1.6%, $p=.11$. Adding both internalizing and externalizing variables (Model D) resulted in an IC of 1.0, $p=.20$.

DISCUSSION

In a representative sample of U.S. adult drinkers, we report two notable findings from our primary analyses. First, the number of stressful life events experienced was associated with increased risk for both moderate and severe alcohol craving. Second, for severe craving, we found evidence for a stress sensitization effect due to childhood adversity, i.e., that the relationship between stressful life events in adulthood and severe craving was exacerbated by a history of childhood maltreatment, as indicated by a risk difference associated with multiple stressful events nearly three times as large among those with childhood maltreatment than among those without childhood maltreatment.

When faced with similar levels of stressful life events, individuals with a history of childhood maltreatment were more likely to experience severe craving than individuals without such a history. This finding suggests that the experience of childhood maltreatment may confer a lasting sensitivity to later stressful life events, and is consistent with prior studies that have found a similar interactive effect on alcohol outcomes including heavy alcohol consumption (Young-Wolff et al., 2012, Keyes et al., 2012) and alcohol use disorders (Keyes et al., 2014). The growing number of adverse outcomes associated with stress sensitivity due to childhood maltreatment identified in the literature highlights a vulnerable population that warrants special attention for prevention and treatment.

In exploratory analyses, the main effects of stressful life events and childhood maltreatment on both moderate and severe alcohol craving remained significant after adding internalizing and externalizing disorders to the models, albeit somewhat attenuated. These results suggested the possibility of partial mediation by psychiatric comorbidity, which should be explored in further studies.

The exploratory analyses adding internalizing and externalizing disorders to the interaction models of stress sensitization suggested that these disorders had a more pronounced and complex relationship to stress sensitization as a risk factor for severe alcohol craving. Addition of internalizing or externalizing disorders diminished the size of the IC to a similar extent. However, when both types of comorbidity were added, the IC was diminished further. Given the greater sample sizes needed to accommodate these additional covariates, these smaller ICs were no longer significant. These results suggest the operation of a more complex mediated moderation model for severe craving, in which stress sensitization may be mediated by both types of psychiatric comorbidity, perhaps with different implications from the influence of internalizing and externalizing disorders for etiology and intervention. Such a model should be investigated in future studies.

Interestingly, addition of internalizing and externalizing disorders appeared to operate in a completely different manner for moderate alcohol craving. Here, risk differences due to stressful life events were larger for those with no history of childhood maltreatment, a discrepancy that grew greater with the addition of internalizing, externalizing and both types

of comorbidity to the models. The lack of significant ICs for moderate craving precludes any firm conclusions, but does suggest the merit of further work to better understand the relationship between proximal stressful life events and moderate alcohol craving.

Study limitations are noted. First, the cross-sectional data preclude establishing temporality. However, by definition, childhood maltreatment preceded the proximal life events and the experience of alcohol craving in the prior 12 months. Further, while alcohol craving could precede the occurrence of stressful life events, clinical studies indicated that stress is a likely precursor to craving (Fox et al., 2007, Sinha et al., 2009). Second, additional factors may be involved in the relationships we investigated. However, our primary analyses incorporated many key control variables, and the exploratory analyses further included several types of psychiatric comorbidity. These results suggested the operation of more complex models, which should be developed further in future studies. Nevertheless, the present study initiates this line of investigation by identifying the contributions of stressful events and their modification by childhood maltreatment, providing a foundation for the development of future models of stress sensitization. Third, those who had abstained from alcohol for at least a year were not asked about past-year alcohol experiences, including craving. While laboratory studies have shown that stress heightens cravings during abstinence in alcohol dependent individuals (Breese et al., 2005), the duration of this phenomenon is unclear. Future studies could investigate whether drinking status (abstention vs. drinking) moderates the relationship between stress and craving and for how long any such effect persists.

Strengths of the study also warrant mention. These include the large, representative sample, (Grant, 2006), inclusion of the alcohol craving items consistent with DSM-5, the ability to control for many potential confounders, and the availability of highly reliable and valid measures (Grant et al., 2003, Ruan et al., 2008). With the addition of a craving criterion to the DSM-5, the current study provides timely evidence of novel associations between childhood maltreatment, stressful life events and alcohol craving in a general population of adult drinkers.

Childhood maltreatment is a potentially preventable exposure that appears to increase the salience of stressors experienced throughout adulthood. Enhanced surveillance and early identification of childhood maltreatment may help prevent the development of stress sensitivity to craving and other adverse outcomes (Hyman et al., 2007). Although craving is increasingly considered a viable target for pharmacological treatments (Kalk and Lingford-Hughes, 2012), our findings are consistent with well-established and effective behavioral intervention techniques (Marlatt and Donovan, 2005, Carroll, 1998) that help patients understand and manage the relationship between stress and craving. Given our results in the general population, public education programs could increase public awareness of the relationship of stress and stress sensitivity to severe alcohol craving, potentially reducing the risk for alcohol problems by suggesting techniques to better manage stress, especially among those most vulnerable to its effects due to adverse childhood exposures.

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References

- AFIFI TO, MATHER A, BOMAN J, FLEISHER W, ENNS MW, MACMILLAN H, SAREEN J. Childhood adversity and personality disorders: results from a nationally representative population-based study. *J Psychiatr Res.* 2011; 45:814–22. [PubMed: 21146190]
- AGRAWAL A, HEATH AC, LYNSKEY MT. DSM-IV to DSM-5: the impact of proposed revisions on diagnosis of alcohol use disorders. *Addiction.* 2011; 106:1935–43. [PubMed: 21631621]
- AMERICAN PSYCHIATRIC ASSOCIATION. *Diagnostic and Statistical Manual of Mental Disorders. Fifth Edition.* American Psychiatric Association; Washington, D.C.: 2013.
- ANDERSSON T, ALFREDSSON L, KALLBERG H, ZDRAVKOVIC S, AHLBOM A. Calculating measures of biological interaction. *Eur J Epidemiol.* 2005; 20:575–9. [PubMed: 16119429]
- ANTON RF. What is craving? *Alcohol research & health.* 1999; 23:165. [PubMed: 10890811]
- BERNSTEIN DP, FINK L, HANDELSMAN L, FOOTE J, LOVEJOY M, WENZEL K, SAPARETO E, RUGGIERO J. Initial reliability and validity of a new retrospective measure of child abuse and neglect. *Am J Psychiatry.* 1994; 151:1132–6. [PubMed: 8037246]
- BREESE GR, CHU K, DAYAS CV, FUNK D, KNAPP DJ, KOOB GF, LÊ DA, O'DELL LE, OVERSTREET DH, ROBERTS AJ, SINHA R, VALDEZ GR, WEISS F. Stress Enhancement of Craving During Sobriety: A Risk for Relapse. *Alcoholism: Clinical and Experimental Research.* 2005; 29:185–195.
- CARROLL, KM. *A Cognitive Behavioral Approach: treating cocaine addiction.* National Institute on Drug Abuse; Rockville, MD: 1998.
- COHEN E, FEINN R, ARIAS A, KRANZLER HR. Alcohol treatment utilization: Findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Drug and Alcohol Dependence.* 2007; 86:214–221. [PubMed: 16919401]
- COMPTON WM, GRANT BF, COLLIVER JD, GLANTZ MD, STINSON FS. Prevalence of marijuana use disorders in the United States: 1991-1992 and 2001-2002. *JAMA.* 2004; 291:2114–21. [PubMed: 15126440]
- DAWSON DA, GRANT BF. Family history of alcoholism and gender: their combined effects on DSM-IV alcohol dependence and major depression. *J Stud Alcohol.* 1998; 59:97–106. [PubMed: 9498321]
- DAWSON DA, GRANT BF, RUAN WJ. The association between stress and drinking: modifying effects of gender and vulnerability. *Alcohol Alcohol.* 2005; 40:453–60. [PubMed: 15972275]
- DE BRUIJN C, VAN DEN BRINK W, DE GRAAF R, VOLLEBERGH WA. Alcohol abuse and dependence criteria as predictors of a chronic course of alcohol use disorders in the general population. *Alcohol Alcohol.* 2005; 40:441–6. [PubMed: 16009673]
- DONG M, ANDA RF, DUBE SR, GILES WH, FELITTI VJ. The relationship of exposure to childhood sexual abuse to other forms of abuse, neglect, and household dysfunction during childhood. *Child Abuse Negl.* 2003; 27:625–39. [PubMed: 12818611]
- DUBE SR, FELITTI VJ, DONG M, CHAPMAN DP, GILES WH, ANDA RF. Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics.* 2003; 111:564–72. [PubMed: 12612237]
- EHLERS CL, GIZER IR, VIETEN C, WILHELMSSEN KC. Linkage analyses of cannabis dependence, craving, and withdrawal in the San Francisco family study. *Am J Med Genet B Neuropsychiatr Genet.* 2010; 153B:802–11. [PubMed: 19937978]
- FENTON MC, GEIER T, KEYES K, SKODOL AE, GRANT BF, HASIN DS. Combined role of childhood maltreatment, family history, and gender in the risk for alcohol dependence. *Psychol Med.* 2013; 43:1045–57. [PubMed: 22883538]
- FOX HC, BERGQUIST KL, HONG K-I, SINHA R. Stress-Induced and Alcohol Cue-Induced Craving in Recently Abstinent Alcohol-Dependent Individuals. *Alcoholism: Clinical and Experimental Research.* 2007; 31:395–403.

- GRANT BF, DAWSON DA, STINSON FS, CHOU PS, KAY W, PICKERING R. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. *Drug and Alcohol Dependence*. 2003; 71:7–16. [PubMed: 12821201]
- GRANT BF, DAWSON DA, STINSON FS, CHOU SP, DUFOUR MC, PICKERING RP. The 12-month prevalence and trends in DSM-IV alcohol abuse and dependence: United States, 1991-1992 and 2001-2002. *Drug Alcohol Depend*. 2004a; 74:223–34. [PubMed: 15194200]
- GRANT BF, DAWSON DA. Introduction to the National Epidemiologic Survey on Alcohol and Related Conditions. *Alcohol Research & Health*. 2006; 29:74–78.
- GRANT BF, GOLDSTEIN RB, CHOU SP, HUANG B, STINSON FS, DAWSON DA, SAHA TD, SMITH SM, PULAY AJ, PICKERING RP, RUAN WJ, COMPTON WM. Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *Mol Psychiatry*. 2009; 14:1051–66. [PubMed: 18427559]
- GRANT BF, HARFORD TC, DAWSON DA, CHOU PS, PICKERING RP. The Alcohol Use Disorder and Associated Disabilities Interview schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. *Drug Alcohol Depend*. 1995; 39:37–44. [PubMed: 7587973]
- GRANT BF, STINSON FS, DAWSON DA, CHOU SP, RUAN WJ, PICKERING RP. Cooccurrence of 12-month alcohol and drug use disorders and personality disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2004b; 61:361–8. [PubMed: 15066894]
- HARKNESS KL, BRUCE AE, LUMLEY MN. The role of childhood abuse and neglect in the sensitization to stressful life events in adolescent depression. *J Abnorm Psychol*. 2006; 115:730–41. [PubMed: 17100530]
- HASIN, DS. Proceedings from APA '13: Substance Use Disorders in DSM-5. American Psychiatric Association Annual Meeting; San Francisco. 2013;
- HASIN DS, O'BRIEN CP, AURIACOMBE M, BORGES G, BUCHOLZ K, BUDNEY A, COMPTON WM, CROWLEY T, LING W, PETRY NM, SCHUCKIT M, GRANT BF. DSM-5 criteria for substance use disorders: recommendations and rationale. *Am J Psychiatry*. 2013; 170:834–51. [PubMed: 23903334]
- HASIN DS, STINSON FS, OGBURN E, GRANT BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2007; 64:830–42. [PubMed: 17606817]
- HICKS BM, KRUEGER RF, IACONO WG, MCGUE M, PATRICK CJ. Family transmission and heritability of externalizing disorders: a twin-family study. *Arch Gen Psychiatry*. 2004; 61:922–8. [PubMed: 15351771]
- HIGLEY AE, CRANE NA, SPADONI AD, QUELLO SB, GOODELL V, MASON BJ. Craving in response to stress induction in a human laboratory paradigm predicts treatment outcome in alcohol-dependent individuals. *Psychopharmacology (Berl)*. 2011; 218:121–9. [PubMed: 21607563]
- HYMAN SM, PALIWAL P, SINHA R. Childhood maltreatment, perceived stress, and stress-related coping in recently abstinent cocaine dependent adults. *Psychol Addict Behav*. 2007; 21:233–8. [PubMed: 17563143]
- KALILANI L, ATASHILI J. Measuring additive interaction using odds ratios. *Epidemiol Perspect Innov*. 2006; 3:5. [PubMed: 16620385]
- KALK NJ, LINGFORD-HUGHES ALH. The Clinical Pharmacology of Acamprosate. *British Journal of Clinical Pharmacology*. 2012 n/a-n/a.
- KENDLER KS, PRESCOTT CA, MYERS J, NEALE MC. The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Arch Gen Psychiatry*. 2003; 60:929–37. [PubMed: 12963675]

- KEYES KM, HATZENBUEHLER ML, HASIN DS. Stressful life experiences, alcohol consumption, and alcohol use disorders: the epidemiologic evidence for four main types of stressors. *Psychopharmacology (Berl)*. 2011a; 218:1–17. [PubMed: 21373787]
- KEYES KM, KRUEGER RF, GRANT BF, HASIN DS. Alcohol craving and the dimensionality of alcohol disorders. *Psychol Med*. 2011b; 41:629–40. [PubMed: 20459881]
- KEYES KM, MCLAUGHLIN KA, KOENEN KC, GOLDMANN E, UDDIN M, GALEA S. Child maltreatment increases sensitivity to adverse social contexts: neighborhood physical disorder and incident binge drinking in Detroit. *Drug Alcohol Depend*. 2012; 122:77–85. [PubMed: 21981990]
- KEYES KM, SHMULEWITZ D, GREENSTEIN E, MCLAUGHLIN K, WALL M, AHARONOVICH E, WEIZMAN A, FRISCH A, SPIVAK B, GRANT BF, HASIN D. Exposure to the Lebanon War of 2006 and effects on alcohol use disorders: The moderating role of childhood maltreatment. *Drug Alcohol Depend*. 2014; 134:296–303. [PubMed: 24262650]
- KNOL MJ, VANDERWEELE TJ, GROENWOLD RH, KLUNGEL OH, ROVERS MM, GROBBEE DE. Estimating measures of interaction on an additive scale for preventive exposures. *Eur J Epidemiol*. 2011; 26:433–8. [PubMed: 21344323]
- KRUEGER RF. The structure of common mental disorders. *Arch Gen Psychiatry*. 1999; 56:921–6. [PubMed: 10530634]
- MARLATT, GA.; DONOVAN, DDM. *Relapse prevention: Maintenance strategies in the treatment of addictive behaviors*. Guilford Press; 2005.
- MAZURE CM. Life Stressors as Risk Factors in Depression. *Clinical Psychology: Science and Practice*. 1998; 5:291–313.
- MCLAUGHLIN KA. Childhood adversity, adult stressful life events, and risk of past-year psychiatric disorder: a test of the stress sensitization hypothesis in a population-based sample of adults. *Psychological medicine*. 2010; 40:1647–1658. [PubMed: 20018126]
- PEER K, RENNERT L, LYNCH KG, FARRER L, GELERNTER J, KRANZLER HR. Prevalence of DSM-IV and DSM-5 alcohol, cocaine, opioid, and cannabis use disorders in a largely substance dependent sample. *Drug Alcohol Depend*. 2013; 127:215–9. [PubMed: 22884164]
- PILOWSKY DJ, KEYES KM, GEIER TJ, GRANT BF, HASIN DS. Stressful Life Events and Relapse Among Formerly Alcohol Dependent Adults. *Soc Work Ment Health*. 2013; 11
- RESEARCH TRIANGLE INSTITUTE. SUDAAN: Professional Software for SURvey DATA ANalysis. RTI; 1989.
- RUAN WJ, GOLDSTEIN RB, CHOU SP, SMITH SM, SAHA TD, PICKERING RP, DAWSON DA, HUANG B, STINSON FS, GRANT BF. The alcohol use disorder and associated disabilities interview schedule-IV (AUDADIS-IV): reliability of new psychiatric diagnostic modules and risk factors in a general population sample. *Drug Alcohol Depend*. 2008; 92:27–36. [PubMed: 17706375]
- SAN JOSÉ B, VAN OERS HAM, VAN DE MHEEN HD, GARRETSEN HFL, MACKENBACH JP. Stressors and alcohol consumption. *Alcohol and Alcoholism*. 2000; 35:307–312. [PubMed: 10869253]
- SINHA R. How does stress increase risk of drug abuse and relapse? *Psychopharmacology (Berl)*. 2001; 158:343–59. [PubMed: 11797055]
- SINHA R. The role of stress in addiction relapse. *Curr Psychiatry Rep*. 2007; 9:388–95. [PubMed: 17915078]
- SINHA R, FOX HC, HONG KA, BERGQUIST K, BHAGWAGAR Z, SIEDLARZ KM. Enhanced negative emotion and alcohol craving, and altered physiological responses following stress and cue exposure in alcohol dependent individuals. *Neuropsychopharmacology*. 2009; 34:1198–208. [PubMed: 18563062]
- SINHA R, LI CSR. Imaging stress- and cue-induced drug and alcohol craving: association with relapse and clinical implications. *Drug and Alcohol Review*. 2007; 26:25–31. [PubMed: 17364833]
- STRAUS, MA.; GELLES, RJ. *Physical violence in American families: Risk factors and adaptations to violence in 8,145 families*. Transaction Publishing; New Brunswick, NJ: 1990.
- WAXMAN R, FENTON MC, SKODOL AE, GRANT BF, HASIN D. Childhood maltreatment and personality disorders in the USA: Specificity of effects and the impact of gender. *Personality and Mental Health*. 2013 n/a-n/a.

YOUNG-WOLFF KC, KENDLER KS, PRESCOTT CA. Interactive effects of childhood maltreatment and recent stressful life events on alcohol consumption in adulthood. *J Stud Alcohol Drugs*. 2012; 73:559–69. [PubMed: 22630794]

Table 1

Prevalence of past-year alcohol craving by socio-demographic subgroup, psychiatric comorbidity, and past-year alcohol dependence in adult Wave 2 NESARC past-year drinkers (n=22,147).

	<i>N</i> <i>a</i>	Prevalence of moderate craving <i>I</i> % (SE) <i>b</i>	p-value	Prevalence of severe craving <i>I</i> % (SE) <i>b</i>	p-value
<u>Total</u>	22,147	3.41 (0.16)		0.84 (<01)	
<u>Sex</u>			<.01		<.01
Male	10,377	4.43 (0.25)		1.11 (0.14)	
Female	11,770	2.31 (0.18)		0.55 (<01)	
<u>Age</u>			<.01		<.01
18-29 years	3,729	5.75 (0.53)		1.70 (0.27)	
30-45 years	7,676	3.74 (0.28)		0.82 (0.13)	
45-65 years	7,662	2.76 (0.22)		0.67 (0.11)	
>65 years	3,080	0.90 (0.17)		0.11 (<.01)	
<u>Ethnicity/Race</u>			0.22		0.28
White	14,028	3.29 (0.19)		0.76 (<.01)	
Black	3,426	3.53 (0.40)		1.27 (0.30)	
Hispanic	3,844	3.52 (0.53)		0.96 (0.24)	
Asian/N.A./Other	849	4.81 (0.94)		1.03 (0.43)	
<u>Educational Attainment</u>			0.06		<.01
Less than high school	2,323	3.80 (0.58)		1.93 (0.37)	
High school/G.E.D. equivalent	5,548	3.07 (0.29)		0.91 (0.16)	
Some college/technical degree	7,515	3.95 (0.30)		0.86 (0.14)	
College or graduate degree	6,761	2.99 (0.27)		0.44 (<.01)	
<u>Parental History of Alcoholism</u>			<.01		<.01
Parental history	5,171	5.22 (0.36)		1.40 (0.21)	
No history	16,976	2.88 (0.17)		0.68 (<.01)	
<u>Any mood/anxiety disorder (past-year)</u>			<.01		<.01
Any past-year disorder	4,065	7.74 (0.54)		2.67 (0.33)	
No past-year disorder	18,082	2.50 (0.15)		0.46 (<.01)	
<u>Antisocial Personality Disorder (lifetime)</u>			<.01		<.01

	<i>N</i> ^a	Prevalence of moderate craving ¹ % (SE) ^b	p-value	Prevalence of severe craving ¹ % (SE) ^b	p-value
Lifetime history	927	9.73 (0.52)		4.36 (0.79)	
No history	21,225	3.12 (0.16)		0.68 (<.01)	
<u>Any Drug Dependence² (past-year)</u>			<.01		<.01
Dependence with or without abuse	226	19.38 (3.23)		14.34 (3.54)	
No dependence	21,926	3.24 (0.16)		0.69 (<.01)	

^aBased on unweighted data.

^bBased on weighted data.

¹Moderate craving was defined as “have you felt a very strong desire to drink?”. Severe craving was defined as “have you ever wanted a drink so badly that you couldnd’t think of anything else?”. Both were measured in the past-year at the Wave 2 assessment.

²Any drug dependence was defined as any past- year diagnosis of substance dependence including sedatives, tranquilizers, opioids, amphetamines, marijuana, hallucinogens, cocaine, inhalants, heroin, and other drugs.

Table 2

Prevalence of stressful life events (SLE) by socio-demographic subgroup, psychiatric comorbidity, history of childhood maltreatment, and past-year alcohol dependence in adult Wave 2 NESARC past-year drinkers (n=22,147).

	<i>N</i> ^a	No Events % (SE) ^b	One to Two SLE % (SE) ^b	Three or more SLE % (SE) ^b	p-value
Total	22,147	52.86 (0.47)	42.28 (0.43)	4.86 (0.21)	
Sex					0.23
Male	10,377	53.53 (0.64)	41.66 (0.58)	4.81 (0.30)	
Female	11,770	52.14 (0.60)	42.95 (0.57)	4.91 (0.24)	
Age					<.01
18-29 years	3,729	44.23 (1.06)	46.49 (1.03)	9.28 (0.59)	
30-45 years	7,676	51.87 (0.73)	42.30 (0.65)	5.83 (0.34)	
45-65 years	7,662	56.28 (0.73)	40.58 (0.73)	3.14 (0.22)	
>65 years	3,080	58.96 (0.98)	40.52 (0.99)	0.52 (0.13)	
Ethnicity/Race					<.01
White	14,028	55.41 (0.55)	40.89 (0.51)	3.70 (0.21)	
Black	3,426	35.42 (1.38)	52.50 (1.28)	12.08 (0.83)	
Hispanic	3,844	49.42 (1.11)	44.06 (1.14)	6.52 (0.64)	
Asian/N.A./Other	849	53.84 (2.49)	40.65 (2.31)	5.51 (0.94)	
Educational Attainment					<.01
Less than high school	2,323	42.02 (1.46)	47.70 (1.41)	10.28 (1.02)	
High school/G.E.D. equivalent	5,548	49.68 (0.77)	44.14 (0.78)	6.18 (0.36)	
Some college/technical degree	7,515	49.93 (0.71)	44.83 (0.65)	5.24 (0.31)	
College or graduate degree	6,761	61.78 (0.76)	36.44 (0.75)	1.77 (0.17)	
Childhood maltreatment					<.01
Previous history	7,321	45.93 (0.74)	46.49 (0.73)	7.58 (0.39)	
No History	14,826	55.99 (0.56)	40.38 (0.53)	3.63 (0.21)	
Parental History of Alcoholism					<.01
Parental history	5,171	45.99 (0.77)	46.74 (0.73)	7.27 (0.48)	
No history	16,976	54.87 (0.54)	40.97 (0.51)	4.16 (0.20)	
Any mood/anxiety disorder (past-year)					<.01
Any past-year disorder	4,065	35.32 (0.96)	53.50 (0.98)	11.18 (0.64)	

	<i>N</i> ^a	No Events % (SE) ^b	One to Two SLE % (SE) ^b	Three or more SLE % (SE) ^b	p-value
No past-year disorder	18,082	56.56 (0.52)	39.91 (0.48)	3.53 (0.18)	
Antisocial Personality Disorder (lifetime)					
Lifetime history	927	31.37 (1.91)	53.70 (2.17)	14.93 (1.57)	<.01
No history	21,220	53.86 (0.47)	41.75 (0.43)	4.39 (0.19)	
Any Drug Dependence² (past-year)					
Dependence with or without abuse	226	12.98 (2.62)	52.31 (4.10)	34.71 (4.33)	
No dependence	21,921	53.30 (0.48)	42.17 (0.43)	4.53 (0.20)	<.01

^aBased on unweighted data.

^bBased on weighted data.

² Any drug dependence was defined as any past-year diagnosis of substance dependence including sedatives, tranquilizers, opioids, amphetamines, marijuana, hallucinogens, cocaine, inhalants, heroin, and other drugs.

Table 3

Main effects of past-year stressful life events and childhood maltreatment on past-year alcohol craving among Wave 2 NESARC past-year drinkers (n=22, 147).

MODERATE CRAVING	N^a	Model A^a OR (95% C.I.)	Model B^b OR (95% C.I.)	Model C^c OR (95% C.I.)	Model D^d OR (95% C.I.)
<u>Stressful life events</u>					
No events	11,320	(reference)	(reference)	(reference)	(reference)
One to two events	9,594	1.53 (1.24-1.90)	1.36 (1.10-1.67)	1.47 (1.19-1.83)	1.32 (1.06-1.63)
Three or more events	1,233	3.15 (2.30-4.33)	2.37 (1.70-3.30)	2.63 (1.87-3.69)	2.09 (1.48-2.96)
<u>Childhood maltreatment</u>					
No history	14,826	(reference)	(reference)	(reference)	(reference)
Previous history	7,321	1.59 (1.28-1.98)	1.37 (1.09-1.72)	1.51 (1.21-1.88)	1.32 (1.05-1.67)
SEVERE CRAVING	N^a	OR (95% C.I.)^a	OR (95% C.I.)^b	aOR^c (95% C.I.)^c	aOR (95% C.I.)^d
<u>Stressful life events</u>					
No events	11,320	(reference)	(reference)	(reference)	(reference)
One to two events	9,594	2.54 (1.58-4.08)	2.10 (1.31-3.37)	2.31 (1.43-3.73)	1.95 (1.21-3.15)
Three or more events	1,233	8.47 (4.78-15.01)	5.72 (3.21-10.19)	5.63 (3.07-10.36)	4.27 (2.32-7.83)
<u>Childhood maltreatment</u>					
No history	14,826	(reference)	(reference)	(reference)	(reference)
Previous history	7,321	2.46 (1.66-3.65)	2.00 (1.30-3.06)	2.20 (1.45-3.33)	1.88 (1.21-2.91)

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; C.I., confidence interval.

^aModel A = adjusted for age, sex, race, education, and includes parental history of alcoholism.

^bModel B = includes all covariates in Model A and internalizing disorders (i.e. past-year mood or anxiety disorders).

^cModel C = includes all covariates in Model A and externalizing disorders (i.e. lifetime history of antisocial personality disorder and past-year drug dependence (marijuana, cocaine, opioids, sedatives, tranquilizers, amphetamines, hallucinogens, inhalants, heroin, other drugs).

^dModel D = includes all covariates in Model A and internalizing and externalizing disorders.

Table 4

Risk differences for alcohol craving at each level of stressful life events experienced by history of childhood maltreatment, among Wave 2 NESARC past-year drinkers (n=22,147).

	History of childhood maltreatment (n=7,321)	No history of childhood maltreatment (n=14,826)	
	Risk difference for <i>mild</i> craving RD % (SE) p-value	Risk difference for <i>mild</i> craving RD % (SE) p-value	Differential effects ¹ IC % (SE) p-value
<i>Model A^a</i>			
No events	(reference)	(reference)	
One to two events	1.6 (0.7) 0.023	1.1 (0.4) 0.002	0.5 (0.7) 0.541
Three or more events	4.0 (1.4) 0.005	6.2 (1.5) <001	-2.2 (2.1) 0.298
<i>Model B^b</i>			
No events	(reference)	(reference)	
One to two events	0.9 (0.6) 0.143	0.8 (0.4) 0.017	0.1 (0.7) 0.943
Three or more events	2.1 (1.1) 0.077	4.9 (1.3) <001	-2.8 (1.8) 0.121
<i>Model C^c</i>			
No events	(reference)	(reference)	
One to two events	1.3 (0.7) 0.051	1.0 (0.4) 0.05	0.3 (0.7) 0.724
Three or more events	2.5 (1.3) 0.059	5.4 (1.4) <001	-2.9 (1.9) 0.130
<i>Model D^d</i>			
No events	(reference)	(reference)	
One to two events	0.7 (0.6) 0.221	0.8 (0.4) 0.029	-0.1 (0.7) 0.937
Three or more events	1.2 (1.1) 0.260	4.4 (1.3) 0.001	-3.2 (1.7) 0.066
	Risk difference for <i>severe</i> craving RD % (SE) p-value	Risk difference for <i>severe</i> craving RD % (SE) p-value	Differential effects ^c IC % (SE) p-value
<i>Model A^a</i>			
No events	(reference)	(reference)	
One to two events	0.9 (0.3) 0.006	0.4 (0.2) 0.012	0.5 (0.4) 0.155
Three or more events	4.6 (1.1) <001	1.7 (0.6) 0.005	2.8 (1.2) 0.017
<i>Model B^b</i>			

	History of childhood maltreatment (n=7,321)	No history of childhood maltreatment (n=14,826)
	Risk difference for mild craving RD % (SE) p-value	Risk difference for mild craving RD % (SE) p-value
No events	(reference)	(reference)
One to two events	0.6 (0.3) 0.035	0.4 (0.2) 0.029
Three or more events	2.8 (0.8) <.001	1.3 (0.5) 0.010
<i>Model C</i>		
No events	(reference)	(reference)
One to two events	0.8 (0.3) 0.015	0.4 (0.2) 0.017
Three or more events	2.8 (0.9) 0.002	1.2 (0.5) 0.013
<i>Model D</i>		
No events	(reference)	(reference)
One to two events	0.6 (0.3) 0.059	0.3 (0.2) 0.040
Three or more events	2.0 (0.7) 0.004	1.0 (0.4) 0.024

Abbreviations: RD, risk differences; IC, interaction contrast (test statistic for differential effects); SE, standard error.

Effects represent expected risk differences if each category of stressful events was fixed to have all of the control variables be equal.

^aModel A = adjusted for age, sex, race, education, and includes parental history of alcoholism

^bModel B = includes all covariates in Model A and internalizing disorders (i.e. past-year mood or anxiety disorders).

^cModel C = includes all covariates in Model A and externalizing disorders (i.e. lifetime history of antisocial personality disorder and past-year drug dependence (marijuana, cocaine, opioids, sedatives, tranquilizers, amphetamines, hallucinogens, inhalants, heroin, other drugs).

^dModel D = includes all covariates in Model A and internalizing and externalizing disorders

^lDifferential effects (i.e. interaction contrast 'IC') is the difference in risk differences.