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Gender differences in the association between internalizing symptoms and craving in methamphetamine users

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Abstract

Objectives—Methamphetamine (MA) users often have substantial psychiatric comorbidities, with nearly a third reporting lifetime mood disorders and over a quarter reporting lifetime anxiety disorders. Female MA users are more likely to endorse depression and anxiety symptoms compared to men. Craving has been related to mood/anxiety symptoms in MA users. To extend the literature on gender differences in MA use disorder, the present study examines the role of gender as a moderator of the relationship between mood/anxiety symptoms and MA craving.

Methods—Participants (N = 203) were non-treatment seeking, current MA users, recruited from the Los Angeles community for enrollment in a larger pharmacotherapy trial. At the assessment visit, participants completed multiple measures including the Methamphetamine Urge Questionnaire, the Beck Depression Inventory, and the Beck Anxiety Inventory.

Results—The relationship between depression symptomatology and MA craving was moderated by gender (F = 6.18, $p = 0.01$), such that the relationship was positive and significant for men ($p < 0.001$) but was not significant for women. Similarly, gender significantly moderated the relationship between anxiety and MA craving ($F = 5.99$, $p = 0.02$), such that the relationship was also positive and significant in men but not in women ($p < 0.001$).

Conclusions—These results suggest that men may be more sensitive to the effects of internalizing symptoms on MA craving than women. Given craving's propensity to predict relapse, these initial findings indicate the necessity of treating comorbid psychiatric problems in male MA users, which may in turn assist in the attenuation of craving.

Keywords

Methamphetamine; Sex/Gender; Craving; Depression; Anxiety

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INTRODUCTION

Methamphetamine (MA) use has a high prevalence with over twelve million people endorsing current use of MA and over half a million individuals meeting criteria for a MA use disorder (MUD) in 2012 (SAMHSA 2014). Multiple studies have demonstrated high rates of psychiatric comorbidities in individuals with MUD. Salo and colleagues (2011) found that 32.3% of those with a MUD had lifetime mood disorder and 26.5% met for lifetime anxiety disorder. In another study, 36% of a MUD sample had current, comorbid psychiatric disorders and being younger, male, and a history of psychiatric disorders were predictive of a current diagnosis (Akindipe et al., 2014).

The Methamphetamine Treatment Project (MTP), a large (n = 526) longitudinal study of MA dependent treatment seekers, provided convincing evidence of significant comorbidities. In this study, 48% of the sample met criteria for an additional Axis I diagnosis, other than substance use disorders, at some point in their lifetime (Glasner-Edwards et al., 2010a). Specifically, 34.2% met criteria for a lifetime mood disorder and 26.2% evidenced a lifetime anxiety disorder (Glasner-Edwards et al., 2010a). Moreover, depression and anxiety diagnoses predicted poorer outcomes and greater impairment in functioning three years post-treatment. Specifically, those with depression and anxiety had poorer MA and alcohol use outcomes, greater overall impairment, higher health service utilization rates, and more psychiatric symptomatology, including higher rates of suicidality (Glasner-Edwards et al., 2009; Glasner-Edwards et al., 2010b).

Gender differences have also been reported in the clinical phenomenology of MUD. However, unlike many other substances, MA is used equally by men and women (Brecht et al., 2004; Durell et al., 2008), a pattern also being observed among alcohol users (White et al., 2015). Brecht and colleagues reported that women often begin using at an earlier age and develop dependence at a quicker rate than men (Brecht et al., 2004). Additionally, differences exist in preferred route of administration, access to MA, and motives for initiation of use, such that men are more likely to prefer smoking or injecting MA, women are more likely to gain access to MA via a significant other, and women are more likely to report initiation of MA use in order to gain energy or lose weight (Brecht et al., 2004). While gender differences have not been observed in treatment seeking behavior, women tend to be retained in treatment longer and have better outcomes (Brecht et al., 2004; Hillhouse et al., 2007; Dluzen & Liu, 2008). Gender differences in psychiatric comorbidity have also been observed, where women with MUD are more likely than men to report symptoms of depression (Hser et al., 2005; Dluzen & Liu, 2008) and meet diagnostic criteria for major depressive disorder (MDD; Glasner-Edwards et al., 2009). Additionally, women with MUD appear more likely to report anxiety (Salo, et al., 2011), particularly social anxiety disorder (Glasner-Edwards et al., 2010a); however, less is known about the treatment of comorbid MUD and mood or anxiety disorders (Hellem, Lundberg, & Renshaw, 2015).

Given that MUD is a complex and heterogeneous phenotype, it has been argued that intermediate phenotypes may be useful in understanding disease pathophysiology and phenomenology. Craving is an important intermediate phenotype of addiction that is predictive of development of a substance use disorder, continued substance use, and

treatment response (Litt et al., 2000; Hartz et al., 2001; Lynch et al., 2002; Bottlender & Soyka, 2004; Sinha et al., 2006). In a sample of MA dependent users, intensity of craving was shown to be predictive of use in the following week such that those in the upper median of craving intensity were at 4.1 higher odds of use (Hartz et al., 2001; Hillhouse et al., 2007). In the MTP sample, craving was also predictive of MA use during the treatment period; however, this relationship diminished over time suggesting that treatment can be impactful at attenuating craving and in turn reducing MA use (Galloway & Singleton, 2009). One study from the MTP sample did not show that craving was a significant predictor of MA use post-treatment (Hillhouse et al., 2007). Yet it has been suggested that the length of MA abstinence post-treatment predicted lower craving scores, with women reporting no craving quicker than men (Galloway et al., 2010). Importantly, craving has also been demonstrated to relate to comorbid psychiatric symptoms in MA users. Negative mood may play a role at potentiating MA craving, as has been shown for other substances (Elman et al., 2002; Zilberman, Tavares, Hodgins, & El-Guebaly, 2007). For example, in a sample of Chinese female MA users in treatment, craving for MA was positively correlated with increased mood disturbance (Shen et al., 2012). Nakama and colleagues (2008) found that in current and past MA users, intensity of craving was positively correlated with greater numbers of depressive symptoms. The latter finding was significant after controlling for abstinence, total grams used/lifetime, duration and frequency of use. A similar finding was observed for the anxiety subscale of the Symptoms Checklist-90 in this study such that intensity of craving positively correlated with reported anxiety (Nakama, et al., 2008).

Taken together, the literature suggests important associations between MA use, craving, and psychiatric comorbidities. Given the clinically meaningful gender differences in MA-related outcomes, such as diagnostic severity, prevalence of comorbidities and treatment response, further exploration of the role of gender as a moderator of the relationship between craving and mood/anxiety symptoms is warranted. Due to the higher likelihood of women with MUD experiencing comorbid mood and anxiety disorders, and the likelihood of comorbid internalizing disorders being strongly correlated with increased craving, it was hypothesized that women MA users would be more affected by internalizing psychiatric symptoms. Specifically, we hypothesize that greater levels of self-reported depression and anxiety would be more strongly related to craving for MA in women as compared to men.

METHODS

Participants and Procedures

Non-treatment seeking MA users (N = 203) were recruited from the Los Angeles community via print and online advertising for a larger study investigating the effect of naltrexone on response to MA (Ray et al., 2015). Participants were invited for an in-person assessment after initial eligibility from a telephone interview was established. During the assessment, informed consent was obtained, participants provided a urine sample for a toxicology screen, and a battery of individual difference measures was completed. Inclusion criteria included: ages 18-50, self-reported use of MA, and fluency in English. Exclusion criteria were: currently in or seeking treatment for MA use, history of bipolar disorder, current major depressive disorder (MDD) with suicidal ideation, or other major psychiatric

disorders, self-reported current use of other drugs (apart from MA, alcohol, tobacco, and marijuana; verified by urine toxicology screens), serious medical conditions or self-reported use of contraindicated medications for the parent study. All study procedures were approved by the Institutional Review Board at UCLA and conformed to the Declaration of Helsinki.

Measures

A demographic questionnaire queried age, ethnicity, marital status, nicotine use, and employment status. Participants completed the MA Urge Questionnaire (MAUQ), an 8-item measure previously adapted from other validated craving measures (Bohn et al., 1995), which assesses craving by level of agreement or disagreement with a series of statements such as “All I want to do now is use methamphetamine” (Ray et al., 2015) on a scale of “0” to “6.” Items are summed to result in a total craving score. The observed Cronbach alpha was 0.87 indicative of reasonable reliability in the present sample. The Beck Depression Inventory-II (BDI-II; Beck et al., 1993), a 21-item measure with total scores ranging from 0-63, was used to assess depressive symptomatology over the previous two weeks. The observed Cronbach alpha for the BDI-II was 0.92 indicative of excellent reliability and comparable to other MA samples (Semple, Zians, Grant & Patterson, 2005). To further explore the facets that make up depressive symptomatology, the BDI-II subscales were also calculated (Dyer & Cruickshank, 2005; Steer et al., 1999); the cognitive-affective subscale, which includes 16 items such as self-criticalness, failure, and guilty feelings, and the somatic subscale, which includes the 5 items related to physical distress, such as changes in appetite, loss of interest in sex, and tiredness. The Beck Anxiety Inventory (BAI; Beck & Steer, 1993), a 21-item measure with total scores ranging from 0-63, was used to assess anxious symptomatology over the previous two weeks. The observed Cronbach alpha for the BAI was 0.92 indicative of excellent reliability. A master's level clinician administered the substance use, depression, mania and psychosis modules of the Structured Clinical Interview for Diagnostic and Statistical Manual for Mental Disorders IV (SCID; First, Spitzer, Gibbon, & Williams, 1995), to assess for MA abuse and dependence diagnosis and the absence of exclusionary disorders (i.e. suicidality, bipolar, psychosis, and current dependence on other substances of abuse) for the parent study, and the Timeline Follow-Back (TLFB; Sobell et al., 1986) to assess frequency and quantity of MA and alcohol use. The MA Withdrawal Questionnaire (MAWQ), a 30-item measure where participants rate withdrawal symptoms on a Likert scale of 0-3 (“Absent” to “Strongly Agree”), was administered to assess the presence and severity of withdrawal symptomatology (Zorick et al., 2010).

Data Analysis Plan

Means, standard deviations, and percentiles were computed for all demographic variables for the whole sample and separately by gender. T-tests and chi square tests were run to assess gender differences. Analyses were run in SAS 9.3 (Cary, NC) using PROC GLM where the dependent measure was MA craving. A series of regression models were conducted wherein the interaction between BDI-II/BAI score and gender was tested. Interaction effects were followed by tests of simple effects to aid in interpreting the direction of the interaction. The total number of symptoms of DSM-IV MA dependence and abuse were summed to create a total symptom count variable, which was used as a covariate in analyses to control for MA

severity. Drinks per drinking day (DPDD) was also included as a covariate to control for gender differences in alcohol use.

RESULTS

Participant Characteristics

Participants were primarily male (71.9%), averaged 35.6 years in age, and unemployed (57.3%; see **Table 1**). The sample's ethnic composition was 31.1% Caucasian, 38.9% Latino, 4.4% Asian, 2.8% Native, and 22.8% African-American. Ethnicity was the only significant gender difference observed in demographic variables ($\chi^2 = 9.7$, $p = 0.05$).

Participants reported using MA on average 20.4 days of the previous 30 days (see **Table 1**), where women reported more days of use than men (22.5 vs. 19.3; t = −2.3, $p = 0.02$). Seventy-six percent of the sample met DSM-IV criteria for MA dependence and 73% met for current abuse. On average, participants met for a mean total of 5.9 current symptoms of the possible 11 total DSM-IV symptoms of dependence and abuse. Participants began using on average at age 22.6 (SD = 8.0). The majority reported smoking (56.2%) as their preferred route of MA administration, which was not significantly different by gender. The average number of drinking days was 8.4 and the average number of DPDD was 4.3, with men reporting significantly more DPDD than women (4.8 vs. 3.3; t = 1.98, $p = 0.05$). Over half the sample reported daily cigarette use (51.6%). Men were more likely to report current marijuana use ($\chi^2 = 4.76$, $p = 0.03$); however, self-reported frequency of use did not significantly differ by gender ($\chi^2 = 6.66$, $p = 0.25$).

Depressive Symptoms and Craving

Participants reported an average total score of 14.0 (SD = 10.9) on the BDI-II, indicative of clinically relevant but mild depression (see **Table 1**; Beck & Steer, 2000). The relationship between depression symptoms and MA craving was significantly moderated by gender (F = 6.18, $p = 0.01$; see **Figure 1**) such that the relationship was significant and positive for men ($r = 0.40$, $p < 0.001$). However, the relationship was not significant for women ($r = 0.01$, NS). Controlling for severity of MA withdrawal symptoms, days since last MA use, having a MA positive urine toxicology, age, or ethnicity did not significantly alter the results reported herein. Removing outlier BDI scores did not significantly alter results ($F = 6.52$, $p = 0.01$). Subsequently, models were tested using the two factor BDI-II structure in order to explore if the relationship was due to increased somatic symptoms (Steer, et al., 1999). First, the cognitive-affective subscale was tested, which held in significance ($F = 8.87$, $p < 0.01$) and direction. Secondly, the somatic subscale was tested, which was not significant ($F = 0.26$, $p > 0.10$).

Anxiety Symptoms and Craving

Participants reported an average total score of 9.9 (SD = 10.0), which is approximately at the mild anxiety cut-off of 10 or greater (Julian, 2011), on the BAI. BAI scores were not significantly different by gender (see **Table 1**). A similar pattern emerged where the interaction of anxiety symptoms and MA craving was significantly moderated by gender ($F = 5.99$, $p = 0.02$; see **Figure 2**) such that the relationship was significant and positive for

men ($r = 0.38$, $p < 0.001$). However, the relationship was not significant for women ($r = 0.01$, NS). Results did not significantly change when controlling for severity of MA withdrawal symptoms, days since last MA use, having a positive urine toxicology for MA, age, or ethnicity, or when removing BAI outlier scores ($F = 4.31$, $p = 0.04$).

DISCUSSION

Despite the known gender differences in psychiatric comorbidities and clinical phenomenology amongst those with MUD, gender differences in MA craving, a known predictor of continued use and relapse, has not previously been explored. Contrary to study hypotheses, the results show that male MA users may be more sensitive to negative internalizing states, as measured by the BDI-II and BAI, in predicting MA craving compared to women. For male MA users, the relationship between depression symptoms and MA craving was positive and significant; however, in female MA users, this relationship was not significant. The same gender pattern was observed for BAI. Similarly, Nakama and colleagues (2008) found that craving was related to greater levels of depression and anxiety in MA users; however, this study did not examine gender differences. Findings presented here are in contrast to those of Shen et al. (2012) who found that increased craving was positively correlated to worsened mood disturbances in female MA users enrolled in treatment. Results of that study may represent the long-term impact of MA use on psychopathology as the female participants had been in a detoxification program for an average of eight months when enrolled in the aforementioned study and may not generalize the results presented herein.

Controlling for MA withdrawal, recency of MA use, toxicology status, age, and ethnicity did not significantly impact findings, suggesting that these gender differences are not the result of participants' mood at the time of assessment and increased craving due to prolonged abstinence. Additionally, depressive symptoms, as captured by the BDI-II, were not due solely to greater somatic symptoms being reported as evinced by the subscale results. Rather, results show that cognitive distress played a larger role in this relationship. This finding aligns with previous work in a sample of MA treatment seekers in Australia whereby MA use was positively related to cognitive symptoms on the BDI-II (Dyer & Cruickshank, 2005).

Despite the relationship observed between mood symptomatology and craving, as well as the mean BDI-II score indicating the sample fell in the mildly depressed range, few participants (n = 11) met DSM-IV criteria for a current major depressive episode. Likewise, the mean BAI score was indicative of mild anxiety. Thus, the data are likely capturing subthreshold distress, which may not be captured by traditional clinical interviewing and diagnostic criteria. This subthreshold distress results in the increased mood disturbance and physiological impact that these measures are designed to capture. Alternatively, the temporal relationship between internalizing symptoms and MA craving cannot be ascertained in this study. Thus, the BDI-II and BAI may be capturing distress produced by long-term MA use or the physical and psychological impact of withdrawal as it is unknown if these symptoms predated the onset of substance use.

The present study results may imply that men may be more vulnerable than women to the effects of internalizing symptoms on MA craving, which may subsequently lead to greater MA use. Alternatively, this sample is made up of non-treatment seekers who did not report the same levels of psychiatric comorbidity as those treatment seeking samples (e.g. MTP sample), and thus, it is possible that the association of internalizing symptoms and craving would be stronger in women in a treatment seeking sample (e.g. Shen et al., 2012) given the higher prevalence of comorbid disorders. For example, in cocaine users, women have been found to report greater craving and depressive symptomatology than men (Elman et al., 2001). Moreover, in a study of treatment seeking, substance dependent participants, Zilberman and colleagues found that depression was a significant predictor of craving in women, but not in men, particularly for alcohol and cocaine users (Zilberman et al., 2007).

The observed relationship between mood/anxiety symptomatology and craving among men has important treatment implications. First, despite the relatively higher rates of anxiety and depressive disorders observed among women compared to men in the general population, the present study suggests that mood and anxiety symptoms may have particular relevance when conceptualizing and treating men with MUD. These symptoms may bear a different relationship to MA craving and relapse than symptom clusters that form the basis of an affective or anxiety disorder diagnosis. As such, coping skills training, which targets management of mild depressive and anxiety symptoms, may be an important component of treatment for men with MA use disorders. Among the effective therapeutic approaches targeting management of negative affect in the context of substance use are: cognitive behavioral therapy (Lee & Rawson, 2008), the Matrix Model (Rawson et al., 2004), and Mindfulness Based Relapse Prevention (Witkiewitz & Bowen, 2010). Some of these treatment approaches have considered tailoring by gender. For example, Shoptaw and colleagues (2005) have developed a CBT based approach for men who have sex with men MA users. Further, Seeking Safety (Najavits et al., 1998) was developed for women with comorbid post-traumatic stress disorder and substance use disorders. Lastly, an eight session supplemental manual has been developed for the implementation of the Matrix Model specifically for women (SAMHSA, 2012). Thus, the present findings that men may be more vulnerable to the effects of internalizing symptoms suggest that employing these techniques, either alone or in combination, could be helpful in mitigating cravings among those with mildly or moderately elevated anxiety and/or depressive symptoms. In turn, it is anticipated that relapse rates might be buffered or improved in the initial post-treatment phase when these interventions are employed.

An additional treatment consideration stemming from the present findings is whether and how the pathway to relapse for women with elevated depressive or anxiety symptoms may be different than it is for men. Negative affect is a common relapse trigger for both genders; however, depressive and anxiety symptoms may lead to MA use in different ways for women, relative to men. For example, men may experience strong urges to use MA in response to negative affect, whereas women may place themselves in risky social situations (i.e., contexts where their peers are drinking or using) as they seek support for coping with negative affect. Understanding the specific trajectories and behaviors that differentiate men from women in their responses to negative affect may be valuable as a means of designing much needed gender-specific interventions (Hellem et al., 2015). For current alcohol users,

women may be more susceptible to alcohol craving in response to negative mood induction than men (Rubonis et al., 1994). After attaining sobriety, evidence suggests that abstinent female alcohol users may be more likely to relapse in response to stress or depression (Snow & Anderson, 2000), though men and women do not differ in relapse rates for alcohol (Walitzer & Dearing, 2006). Thus, there has been a growing interest in integrating these differing needs into treatment to apply gender specific therapies (Beckman, 1994; Hodgins, El-Guebaly, & Addington, 1997).

The study should be interpreted in the context of its strengths and limitations. This study examines a large, community sample of current and regular MA users. The majority of measures utilized in the sample are well-validated and widely used in clinical populations and community samples. Further, a multi-question measure was used to assess MA craving, which may better evaluate craving than reliance on the single-item Visual Analog Scale, as is commonly employed. Limitations of the study include the retrospective design; therefore speculation on causation of this relationship is restricted. Additionally, the SCID administration did not include assessment of anxiety disorders. Thus, comparison of distress due to anxious symptomatology to clinical diagnosis is not possible. The BDI-II and BAI instruct participants to rate symptom severity for the past two weeks whereas the MAUQ captures craving “in the present moment,” thus, there may be temporal effects influencing results. Causal inferences cannot be made as the temporal relationship between internalizing symptoms and MA use in the sample is unknown. The same is true for internalizing symptoms and craving whereby the relationship may be such that craving increases feelings of anxiety and depression. Longitudinal and/or microlongitudinal designs are needed to fully ascertain this causal chain. As depression and anxiety often co-occur (Gorman, 1996), it is possible the two measures are capturing similar distress and do not represent wholly unique dimensions. Depression and psychosis are also known to accompany MA intoxication and acute withdrawal (Zorick, et al., 2010). Though measures of internalizing symptoms had high reliability in this study, few others have examined the reliability and validity of such measures in MA using samples. Valid and accurate assessment of internalizing symptoms in this population is complicated by the fact that mood disturbance and increased anxiety often overlap conceptually with signs and symptoms of MA withdrawal (McGregor et al., 2005; Newton et al., 2004); however, some have argued that withdrawal related mood disturbance generally abates within two weeks of abstinence (Newton et al., 2004; Zorick et al., 2010). Moreover, the average time since last MA use was approximately one day, leading to greater confidence that these findings are not the direct result of withdrawal symptomatology. As may be the case with multiple self-report measures, craving scores may have been influenced or elevated due to a multitude of factors including the stress of being in the laboratory, and reporting bias. Exploration of MA-induced psychosis (McKetin, McLaren, Lubman & Hides, 2006), which may impact internalizing symptomatology (Chen et al., 2003), should be included in future studies. For women, craving scores may have been impacted by hormonal shifts due to the menstrual cycle (Terner & de Wit, 2006). For example, in one study that included administration of D-amphetamine, women in the follicular phase reported greater liking and wanting of the drug than women in the luteal phase (Justice & de Wit, 1999). Thus future studies should carefully consider the role of menstrual cycle hormones on the subjective effects of psychostimulants, including MA.

In conclusion, this study investigated the role of gender in the association of internalizing symptoms and MA craving. This relationship may contribute to the role craving plays in continued MA use in men, particularly as men displayed greater sensitivity to changes in mood and anxiety. Future work should examine if this relationship holds in treatment seeking MA users. Meaningful clinical interventions have been developed for the treatment of MUD; however, these interventions may benefit from the incorporation of better assessments of sub-clinical distress and craving, and the inclusion of psychosocial interventions that address such distress.

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References

Akindipe T, Wilson D, Stein DJ. Psychiatric disorders in individuals with methamphetamine dependence: prevalence and risk factors. Metab Brain Dis. 2014; 29:351–357. [PubMed: 24532047]

Beck, AT.; Steer, RA. Beck anxiety inventory: manual. Psychological Corporation; San Antonio: 1993.

Beck, AT.; Steer, RA. Beck Depression Inventory.. In: Rush, AJ.; Pincus, HA.; First, MB.; Blacker, J.; Endicott, JK., editors. Handbook of Psychiatric Measures. American Psychiatric Association; Washington, D.C.: 2000.

Beck, AT.; Steer, RA.; Brown, GK. Manual for Beck depression inventory-II. Psychological Corporation; San Antinio: 1993.

Beckman LJ. Treatment needs of women with alcohol problems. Alcohol Health Res World. 1994; 18:206–206.

Bohn MJ, Krahn DD, Staehler BA. Development and initial validation of a measure of drinking Urges in Abstinent Alcoholics. Alcohol Clin Exp Res. 1995; 19:600–606. [PubMed: 7573780]

Bottlender M, Soyka M. Impact of craving on alcohol relapse during, and 12 month following, outpatient treatment. Alcohol Alcohol. 2004; 39:357–361. [PubMed: 15208171]

Brecht ML, O'Brien A, Von Mayrhauser C, Anglin MD. Methamphetamine use behaviors and gender differences. Addict Behav. 2004; 29:89–106. [PubMed: 14667423]

Chen CK, Lin SK, Sham PC, Ball D, Loh EW, Hsiao CC, Chiang YL, Ree SC, Lee CH, Murray RM. Pre-morbid characteristics and co-morbidity of methamphetamine users with and without psychosis. Psychol Med. 2003; 33:1407–1414. [PubMed: 14672249]

Dluzen DE, Liu B. Gender differences in methamphetamine use and responses: a review. Gender Med. 2008; 5:24–35.

Durell TM, Kroutil LA, Crits-Christoph P, Barchha N, Van Brunt DL. Prevalence of nonmedical methamphetamine use in the United States. Subst Abuse Treat Prev Policy. 2008; 3:19–29. [PubMed: 18655714]

Dyer KR, Cruickshank CC. Depression and other psychological health problems among methamphetamine dependent patients in treatment: Implications for assessment and treatment outcome. Australian Psychologist. 2005; 40:96–108.

Elman I, Karlsgodt KH, Gastfriend DR. Gender differences in cocaine craving among non-treatment-seeking individuals with cocaine dependence. Am J Drug Alcohol Abuse. 2001; 27:193–202. [PubMed: 11417935]

Elman I, Karlsgodt KH, Gastfriend DR, Chabris CF, Breiter HC. Cocaine-primed craving and its relationship to depressive symptomatology in individuals with cocaine dependence. J Psychopharmacol. 2002; 16:163–167. [PubMed: 12095075]

First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JB. Structured Clinical Interview for DSM-IV Axis I Disorders. Patient Edition. Biometrics Research Department, New York State Psychiatric Institute; New York: Jan. 1995 1995 FINAL: SCID-I/P.

Galloway GP, Singleton EG. How long does craving predict use of methamphetamine? Assessment of use one to seven weeks after the assessment of craving: Craving and ongoing methamphetamine use. Subst Abuse. 2009; 1:63–79. [PubMed: 19898674]

Galloway GP, Singleton EG, Buscemi R, Baggott MJ, Dickerhoof RM, Mendelson JE. An examination of drug craving over time in abstinent methamphetamine users. Am J Addict. 2010; 19:510–514. [PubMed: 20958846]

Glasner-Edwards S, Marinelli-Casey P, Hillhouse M, Ang A, Mooney LJ, Rawson R. Depression among methamphetamine users: Association with outcomes from the Methamphetamine Treatment Project at 3-year follow-up. J Nerv Ment Dis. 2009; 197:225–231. [PubMed: 19363377]

Glasner-Edwards S, Mooney LJ, Marinelli-Casey P, et al. Psychopathology in methamphetamine-dependent adults 3 years after treatment. Drug Alcohol Rev. 2010a; 29:12–20. [PubMed: 20078677]

Glasner-Edwards S, Mooney LJ, Marinelli-Casey P, et al. Anxiety disorders among methamphetamine dependent adults: Association with post-treatment functioning. Am J Addict. 2010b; 19:385–390. [PubMed: 20716300]

Gorman JM. Comorbid depression and anxiety spectrum disorders. Depress Anxiety. 1996; 4:160–168. [PubMed: 9166648]

Hartz DT, Frederick-Osborne SL, Galloway GP. Craving predicts use during treatment for methamphetamine dependence: A prospective, repeated-measures, within-subject analysis. Drug Alcohol Depen. 2001; 63:269–276.

Hellem TL, Lundberg KJ, Renshaw PF. A review of treatment options for co-occurring methamphetamine use disorders and depression. J Addict Nurs. 2015; 26:14–23. [PubMed: 25761159]

Hillhouse MP, Marinelli-Casey P, Gonzales R, Ang A, Rawson RA, the Methamphetamine Treatment Project Corporate Authors. Predicting in-treatment performance and post-treatment outcomes in methamphetamine users. Addiction. 2007; 102:84–95. [PubMed: 17493057]

Hodgins DC, El-Guebaly N, Addington J. Treatment of substance abusers: single or mixed gender programs? Addiction. 1997; 92:805–812. [PubMed: 9293039]

Hser YI, Evans E, Huang YC. Treatment outcomes among women and men methamphetamine abusers in California. J Subst Abuse Treat. 2005; 28:77–85. [PubMed: 15723735]

Julian LJ. Measures of Anxiety. Arthrit Care Res. 2011; 63:1–11.

Justice AJH, de Wit H. Acute effects of d-amphetamine during the follicular and luteal phases of the menstrual cycle in women. Psychopharm. 1999; 145:67–75.

Lee NK, Rawson RA. A systematic review of cognitive and behavioural therapies for methamphetamine dependence. Drug Alcohol Rev. 2008; 27:309–317. [PubMed: 18368613]

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]

Lynch W, Roth M, Carroll M. Biological basis of sex differences in drug abuse: preclinical and clinical studies. Psychopharmacology. 2002; 164:121–137. [PubMed: 12404074]

McGregor C, Srisurapanont M, Jittiwutikarn J, Laobhripatr S, Wongtan T, White JM. The nature, time course and severity of methamphetamine withdrawal. Addiction. 2005; 100:1320–1329. [PubMed: 16128721]

McKetin R, McLaren J, Lubman DI, Hides L. The prevalence of psychotic symptoms among methamphetamine users. Addiction. 2006; 101:1473–1478. [PubMed: 16968349]

Nakama H, Chang L, Cloak C, Jiang C, Alicata D, Haning W. Association between psychiatric symptoms and craving in methamphetamine users. Am J Addict. 2008; 17:441–446. [PubMed: 18770088]

Newton TF, Kalechstein AD, Duran S, Vansluis N, Ling W. Methamphetamine abstinence syndrome: Preliminary findings. Am J Addict. 2004; 13:248–255. [PubMed: 15370944]

Rawson RA, Marinelli-Casey P, Anglin MD, et al. A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence. Addiction. 2004; 99:708–717. [PubMed: 15139869]

Ray LA, Bujarski S, Courtney KE, et al. The effects of naltrexone on subjective response to methamphetamine in a clinical sample: A double-blind, placebo-controlled laboratory study. Neuropsychopharmacology. 2015; 40:2347–2356. [PubMed: 25801501]

Rubonis AV, Colby SM, Monti PM, Rohsenow DJ, Gulliver SB, Sirota AD. Alcohol cue reactivity and mood induction in male and female alcoholics. J Stud Alcohol. 1994; 55:487–494. [PubMed: 7934057]

Substance Abuse and Mental Health Services Administration. Using Matrix with Women Clients: A Supplement to the Matrix Intensive Outpatient Treatment for People with Stimulant Use Disorders. Substance Abuse and Mental Health Services Administration; Rockville, MD: 2012. HHS Pub. No. (SMA) 12-4698

Salo R, Flower K, Kielstein A, Leamon MH, Nordahl TE, Galloway GP. Psychiatric comorbidity in methamphetamine dependence. Psychiat Res. 2011; 186:356–361.

Semple SJ, Zians J, Grant I, Patterson TL. Impulsivity and methamphetamine use. J Subst Abuse Treat. 2005; 29:85–93. [PubMed: 16135337]

Shen W, Liu Y, Li L, Zhang Y, Zhou W. Negative moods correlate with craving in female methamphetamine users enrolled in compulsory detoxification. Subst Abuse Treat Prev Policy. 2012; 7:44–52. [PubMed: 23110820]

Shoptaw S, Reback CJ, Peck JA, Yang X, Rotheram-Fuller E, Larkins S, Veniegas RC, Freese TE, Huck-Ortiz C. Behavioral treatment approaches for methamphetamine dependence and HIV-related sexual risk behaviors among urban gay and bisexual men. Drug Alcohol Depend. 2005; 78:125–134. [PubMed: 15845315]

Sinha R, Garcia M, Paliwal P, Kreek M, Rounsaville B. Stress-induced cocaine craving and hypothalamic-pituitary-adrenal responses are predictive of cocaine relapse outcomes. Arch Gen Psychiatry. 2006; 63:324–331. [PubMed: 16520439]

Snow D, Anderson C. Exploring the factors influencing relapse and recovery among drug and alcohol addicted women. J Psychosoc Nurs Ment Health Serv. 2000; 38:8–19.

Sobell MB, Sobell LC, Klajner F, Pavan D, Basian E. The reliability of a timeline method for assessing normal drinker college students' recent drinking history: utility for alcohol research. Addict Behav. 1986; 11:149–161. [PubMed: 3739800]

Steer RA, Ball R, Ranieri WF. Dimensions of the Beck Depression Inventory-II in clinically depressed outpatients. J Clin Psychol. 1999; 55:117–128. [PubMed: 10100838]

Terner JM, de Wit H. Menstrual cycle phase and responses to drugs of abuse in humans. Drug Alcohol Depend. 2006; 84:1–13. [PubMed: 16413143]

Walitzer KS, Dearing RL. Gender differences in alcohol and substance use relapse. Clin Psychol Rev. 2006; 26:128–148. [PubMed: 16412541]

White A, Castle IJP, Chen CM, Shirley M, Roach D, Hingson R. Converging Patterns of Alcohol Use and Related Outcomes Among Females and Males in the United States, 2002 to 2012. Alcohol Clin Exp Res. 2015; 39:1712–1726. [PubMed: 26331879]

Witkiewitz K, Bowen S. Depression, craving, and substance use following a randomized trial of mindfulness-based relapse prevention. J Consult Clin Psychol. 2010; 78:362–272. [PubMed: 20515211]

Zilberman ML, Tavares H, Hodgins DC, El-Guebaly N. The impact of gender, depression, and personality on cravings. J Addict Dis. 2007; 26:79–84.

Zorick T, Nestor L, Miotto K, et al. Withdrawal symptoms in abstinent methamphetamine-dependent subjects. Addiction. 2010; 105:1809–1818. [PubMed: 20840201]

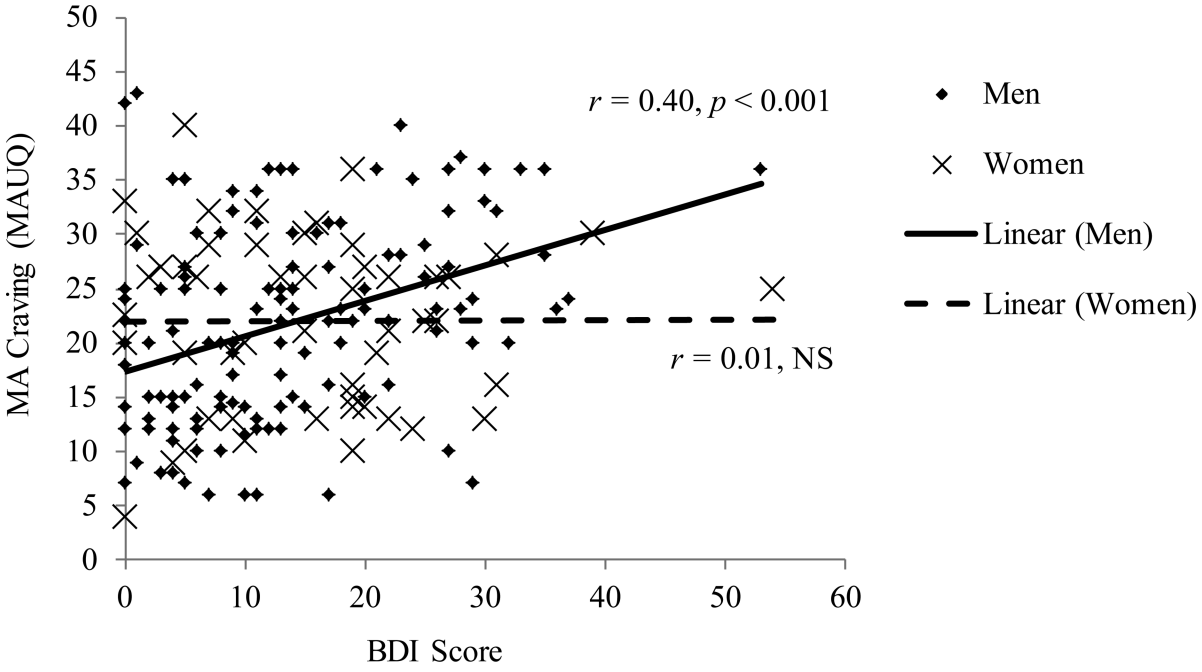

Figure 1.
Regression model of raw BDI-II scores predicting MA craving by gender. Correlation of BDI-II score and craving for each gender is shown.

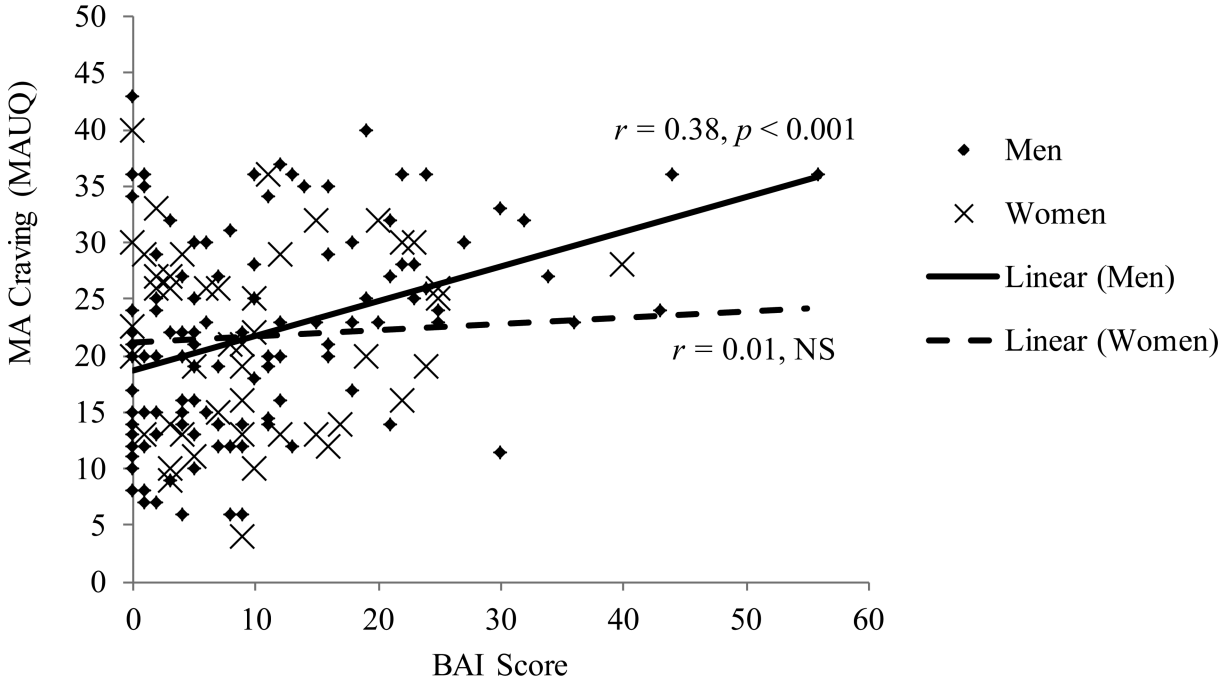

Figure 2.
Regression model of raw BAI scores predicting MA craving by gender. Correlation of BAI score and craving for each gender is shown.

Table 1

Demographic, substance use, and mood variables for the total sample and each gender

	Total (N=203)	Men (N=143)	Women (N = 56)
Demographic Variables			
Age, M(SD)	35.6 (8.8)	35.6 (8.5)	35.7 (9.5)
Years of Education, M(SD)	12.6 (3.1)	12.5 (3.4)	12.8 (2.0)
Ethnicity			
Caucasian, %(N)	31.1 (56)	25.4 (33)	46.0 (23)
African American, %(N)	22.8 (41)	25.4 (33)	16.0 (8)
Asian, %(N)	4.4 (8)	6.2 (8)	0 (0)
Latino, %(N)	38.9 (70)	40 (52)	36.0 (18)
Native American, %(N)	2.8 (5)	3.1 (4)	2.0 (1)
Unemployed, %(N)	57.3 (106)	55.2 (74)	62.7 (32)
Substance Use Variables			
Age of first MA use, M(SD)	22.6 (8.0)	23.0 (8.1)	21.6 (8.0)
Current MA Dependent, %(N)	156 (76.8)	109 (84.5)	47 (90.4)
Total # of DSM-IV MA symptoms, M(SD)	5.9 (2.44)	5.8 (2.5)	6.0 (2.3)
MA Urge Questionnaire, M(SD)	21.8 (8.7)	21.8 (9.0)	22.0 (7.9)
Number days using MA in past 30, M(SD)	20.4 (8.7)	19.3 (8.8)	22.5 (8.0)
Days since last MA use, M(SD)	1.6 (3.6)	2.0 (3.9)	0.8 (2.4)
Smoking as preferred route of MA administration, % (N)	56.2 (114)	73.1 (79)	77.8 (35)
Daily cigarette users, %(N)	51.6 (96)	50.0 (67)	55.8 (29)
Drinks per drinking day, M(SD)	4.3 (3.3)	4.6 (3.5)	3.3 (2.3)
Drinking days, M(SD)	8.4 (10.9)	8.0 (10.2)	7.8 (11.4)
Current marijuana use, %(N)	43.5 (80)	48.5 (64)	30.8 (16)
Mood Variables			
Current Major Depressive Disorder, %(N)	5.4 (11)	4.9 (7)	7.1 (4)
Beck Depression Inventory-II, M(SD)	14.0 (10.9)	13.6 (10.8)	15.0 (11.1)
Beck Anxiety Inventory, M(SD)	9.9 (10.0)	9.9 (9.0)	10.0 (8.8)

*Items in bold signify $p < 0.05$