Published in final edited form as:
J Dual Diagn. 2013 April 1; 9(2): 123–128. doi:10.1080/15504263.2013.779157.

Does Posttraumatic Stress Disorder (PTSD) Affect Post-Treatment Methamphetamine Use?

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Abstract

Objective—Although trauma is a well-established risk factor for substance use disorders, little is known about the association between posttraumatic stress disorder (PTSD) and treatment outcomes among methamphetamine users. In the present study, we examine the relationship between PTSD and post-treatment methamphetamine use outcomes, hospitalizations, and overall psychiatric impairment.

Methods—Using data from 526 adults in the largest psychosocial clinical trial of methamphetamine users conducted to date, this study examined: (1) treatment outcomes of methamphetamine users with concomitant PTSD three years after psychosocial treatment for methamphetamine dependence; and (2) PTSD symptom clusters as risk factors for post-treatment relapse to methamphetamine use.

Results—PTSD was associated with poorer methamphetamine use outcomes; methamphetamine use frequency throughout the 3-year follow-up was significantly greater among individuals with a PTSD diagnosis, and those with PTSD had more than five times the odds of reporting methamphetamine use in the 30 days prior to the follow-up interview, *OR*= 5.2, 95% CI [2.0–13.3]. Additionally, higher levels of other Axis I psychopathology were observed among methamphetamine users with PTSD. Avoidance and arousal symptoms predicted post-treatment methamphetamine use.

Conclusions—Addressing these high risk PTSD symptoms and syndromes in methamphetamine users may be helpful as a means of improving treatment outcomes in this population.

Keywords

methamphetamine; treatment; comorbidity; outcome; PTSD

A wealth of research has linked posttraumatic stress disorder (PTSD) with the use and abuse of a variety of substances, including alcohol, marijuana, stimulants, and opioids (Mills et al., 2006; Sareen et al., 2006), and, individuals with PTSD report elevated rates of substance

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*Methamphetamine Treatment Project Corporate authors are listed in acknowledgments at the end of the manuscript.

A subset of the data presented in this paper was presented at the 74th Annual Meeting of the College on Problems of Drug Dependence, June 9th–14th, 2012, in Palm Springs, California.

DISCLOSURES
The authors report no financial relationships with commercial interests and do not have any additional income to report.

dependence (Kessler et al., 2005; Jacobsen et al., 2001; see Berenz & Coffey, 2012 for review). According to recent work, higher rates of crystal methamphetamine use are observed among those with, versus without, PTSD (Smith et al., 2010). Likewise, stimulants are among the most commonly abused substances in individuals with PTSD history (Mills, 2009). These findings are consistent with an emerging literature suggestive of a strong relationship between PTSD and stimulant use disorders (Back et al., 2000; Brady, 2001; Khoury, Tang, Bradley, Cubells, & Ressler, 2010). Nevertheless, no studies to date have described the association of PTSD with treatment outcomes of methamphetamine users.

Methamphatmine users frequently endorse trauma exposure and/or associated symptoms (see Zweben et al., 2004; Smith et al., 2010). If the impact of these symptoms on outcomes from addiction treatment is consistent with that observed for other substances of abuse, including stimulants, the co-occurrence of PTSD and methamphetamine dependence would have important clinical and treatment implications. Substance users with PTSD evidence accelerated relapse after residential treatment (Brown et al., 1996), greater severity of both disorders, lower functioning, poorer well-being and prognosis, and worse outcomes across a variety of domains, relative to individuals with either disorder alone (Brady, 2001; Schafer & Najavits, 2007). Although the literature documenting this robust relationship between PTSD and poorer prognosis and outcomes includes studies of cocaine users (Ouimette et al., 2010; Saladin et al., 2003), the implications of comorbid PTSD for treatment outcomes of methamphetamine users have not been established.

Recent evidence suggests that specific PTSD symptom clusters are associated with substance dependence severity (Tull et al., 2010), with at least one investigation demonstrating a relationship between avoidance and arousal symptoms and lifetime methamphetamine use frequency (Smith et al., 2010). A handful of studies suggest that PTSD symptom profiles vary as a function of primary substance of abuse among those with PTSD and substance abuse comorbidity (Back, Sonne, Killeen, Dansky, & Brady, 2003). Specifically, drug users exposed to trauma demonstrate relatively elevated hyperarousal (Sullivan & Holt, 2008), and both cocaine and methamphetamine users with PTSD show elevations in both hyperarousal and avoidance symptoms (Najavits et al., 2003; Smith et al., 2010). Whether these clusters of symptoms differentially predict substance use outcomes after addiction treatment is as yet unknown.

The aim of the present study was to replicate and extend the work of Smith et al. (2010) in a clinical sample of individuals with methamphetamine dependence, thereby characterizing the association of PTSD symptom clusters and diagnoses with treatment outcomes. In a study of psychiatric disorders in individuals with methamphetamine dependence three years after psychosocial treatment, anxiety disorders were associated with increased methamphetamine use and poorer functional, health and psychiatric outcomes (Glasner-Edwards et al., 2010). However, associations between specific anxiety disorders and outcomes were not evaluated; thus, the present study evaluates the clinical outcomes of concomitant PTSD in this same cohort of methamphetamine users. A second aim was to evaluate whether prior findings of an association between PTSD symptom clusters and stimulant use severity would be replicated in relationship with post-treatment methamphetamine use. We hypothesized that PTSD would be associated with greater psychiatric comorbidity and impairment (i.e., suicidality), post-treatment stimulant use and hospitalizations relative to those without PTSD.

METHODS

Subjects

Participants were 526 adults with methamphetamine dependence who took part in the Methamphetamine Treatment Project, a randomized, controlled trial of psychosocial treatments for methamphetamine dependence described elsewhere (see Rawson et al., 2004 for full description of the treatments and original sample). Treatment-seeking methamphetamine users, 18 years of age and older, were recruited from outpatient treatment programs in California, Montana, and Hawaii. Individuals were excluded if they exhibited medical or psychiatric impairment that compromised their safety and/or required primary treatment (e.g., hospitalization), or required medical detoxification from any substances. The present follow-up study, conducted using a subset of participants who provided consent to be contacted for subsequent studies (N=672; 66% of the original sample), was approved by the UCLA IRB and the IRBs at each of the respective Methamphetamine Treatment Project study sites, and was conducted in accordance with the Declaration of Helsinki. After a complete discussion of the study, a total of 587 people (87% of the 672) consented to participate in the follow-up study, which comprised medical, psychiatric, and psychosocial assessments. Of those, 61 did not complete the psychiatric interview for various reasons, including having moved out of the area, constraints due to incarceration, inability to schedule a convenient appointment, and/or declining this portion of the assessment. Thus, the final sample included 526 participants. The sample was assessed at baseline and treatment discharge as part of the original study, and then again at a mean of 3.1 years post-treatment (SD=0.48) as part of this follow-up study.

Procedures and Instruments

Trained interviewers conducted assessments at baseline, discharge and follow-up. Methamphetamine use frequency in the 30 days prior to each study visit was assessed using the Addiction Severity Index (McLellan, Luborsky, Woody, & O'Brien, 1980). The Life Experiences Timeline interview (LET; Hillhouse, Marinelli-Casey, & Rawson, 2005) was used to quantify months during which methamphetamine use occurred in the follow-up period. The LET, a measure adapted from the Natural History Interview (Hser, Hoffman, Grella, & Anglin, 2001) assesses substance use history using a month-by-month timeline that links substance use to life events. At treatment discharge, participants also provided a urine sample which was analyzed for the presence of methamphetamine.

The Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998), a brief structured diagnostic interview for assessing DSM-IV psychiatric disorders was administered at follow-up. The MINI assesses affective, anxiety, substance use, eating, and psychotic disorders, and antisocial personality disorder. All interviewers were trained to criterion on the MINI using standardized procedures including didactic instruction, practice interviews, and direct observation. The MINI provided information concerning PTSD symptom clusters; responses to dichotomous items assessing symptoms in each of the three domains (avoidance, arousal, re-experiencing) were summed to create symptom cluster scores for each participant. The MINI also provided information concerning lifetime suicide attempts.

In a separate self-report assessment, participants were asked to report the incidence and number, if any, of hospitalizations in the 12 months prior to follow-up.

Statistical Analysis

Methamphetamine use was indicated by: (1) use in the 30 days preceding follow-up, measured using the ASI (0 = no use; 1= use on one or more days); and (2) number of

months during which use occurred in the follow-up period, measured by the LET. Chi-square and *t*-tests were used to analyze group differences (i.e., comparing those with versus without PTSD) on key outcome variables. Subsequently, multivariate logistic regression analyses were employed to examine the effects of PTSD diagnosis on post-treatment stimulant use, and the relationship between methamphetamine use and psychopathology. Linear regression analyses were conducted to explore whether PTSD symptom clusters predicted post-treatment methamphetamine use.

RESULTS

The original study sample (N=1016) was compared with the subset of participants who were included in the current investigation (N=526) using *t*-tests and chi-square tests for age, education, gender, marital status, route of methamphetamine administration, employment, and baseline ASI composite scores. In all analyses, there were no significant differences between the patients in the current study and the original sample.

Demographic characteristics of the original study sample are described elsewhere (Rawson et al., 2004). At 3-year follow-up, the sample was predominantly female, Caucasian, employed, and high school educated (see Table 1 for complete demographics and baseline methamphetamine use characteristics). There were no differences in demographic or substance use characteristics among those who completed the psychiatric assessment (N=526) relative to those who did not (n=61).

Of the 526 participants, 5.9% (n=31) met criteria for current PTSD at 3-year follow-up. PTSD was diagnosed in 6.9% of women versus 4.3% of men in the sample, a difference that was not statistically significant. Self-reported methamphetamine use frequency during 3-year follow-up was significantly higher among those with (M=20.9 months, SD=14.1) versus without (M=13.7 months, SD=14.0) PTSD, $t(520)=-2.78$, $p<0.01$. In addition, a significantly greater proportion of those with PTSD (67.7%, n=21) reported methamphetamine use in the 30 days preceding follow-up relative to those without a PTSD diagnosis (27.5%, n=136), $\chi^2=22.5$, $df=1$, $p<.0001$).

To examine the potential effects of PTSD on post-treatment methamphetamine use during the follow-up period, a multivariate logistic regression model was used, controlling for demographics, the presence of other Axis I disorders, and route of methamphetamine administration. In this analysis, post-treatment methamphetamine use frequency increased as a function of PTSD diagnosis, $\beta=6.8$, $SE=2.8$; $p<0.05$, $R^2=0.19$. Likewise, while urine toxicology results showed a non-significant difference (albeit in the predicted direction) in the proportion of those with and without PTSD testing negative for methamphetamine at treatment discharge (61% versus 71%, respectively); those with PTSD had more than five times the odds of reporting methamphetamine use in the 30 days prior to follow-up, OR= 5.2, 95% CI [2.0–13.3], with 11% of the variance in outcome explained by the regression model ($R^2=0.11$).

Linear regression analyses revealed that methamphetamine use frequency over the follow-up period varied as a function of PTSD symptom clusters, with higher levels of use predicted by avoidance ($\beta=1.58$, $SE=0.58$; $p<0.01$) and arousal ($\beta=1.50$, $SE=0.62$; $p<0.05$) symptoms, but not re-experiencing the traumatic event.

Relative to those without PTSD, individuals who had PTSD were more likely to have an additional Axis I disorder, with greater proportions of individuals in this subgroup meeting criteria for mood (87.1%, n=27 versus 31.0%, n=153, $\chi^2=40.8$, $df=1$, $p<.0001$), psychotic (45.2%, n=14 versus 10.9%, n=54, $\chi^2=30.3$, $df=1$, $p<.0001$), and eating (12.9%, n=4 versus 1.8%, n=9, $\chi^2=14.8$, $df=1$, $p<.0001$) disorders. Moreover, participants with PTSD had nearly

four times the odds of having attempted suicide once or more in their lifetime, *OR*=3.8, 95% CI [1.8–8.3]. Nevertheless, no difference was observed between those with and without PTSD in the likelihood of having been hospitalized within the year prior to follow-up.

DISCUSSION

This is the first study to examine the relationship between PTSD and treatment outcomes in a large cohort of adults with methamphetamine dependence. In this study, comorbid PTSD was associated with greater methamphetamine use frequency during the three years after treatment. Consistent with Smith et al.'s (2010) findings of an association between lifetime crystal methamphetamine use and PTSD symptom clusters, avoidance and arousal, but not re-experiencing, predicted post-treatment methamphetamine use. Several theories have been advanced to explain the association between PTSD and substance use disorders. The theory that has perhaps the most relevance to understanding how PTSD influences addiction treatment outcomes is the self-medication hypothesis (Khantzian, 1997), which suggests that substances are used to self-medicate PTSD symptoms. This theory is somewhat counterintuitive to the present findings, given that methamphetamine should be expected to increase symptoms of arousal and anxiety more generally. Nevertheless, the intensity and pervasive nature of cravings for methamphetamine (particularly in the presence of negative affective states), observed both clinically and in laboratory settings (see Zorick et al., 2010), may account, in part, for the present findings in individuals with methamphetamine dependence, regardless of the anxiogenic effects of the substance. Moreover, methamphetamine users with PTSD may paradoxically feel safer and in greater control in some situations or environments when hypervigilance (i.e., arousal) is intensified. In addition, in light of the observation that cocaine users with PTSD are more likely to use in pleasant social situations (Waldorp, Back, Berduin, & Brady, 2007) relative to those without PTSD, it is possible that individuals with PTSD and methamphetamine dependence experience greater social confidence or facilitation when using. Finally, it is important to note that despite the specific triggers for methamphetamine use in the presence of PTSD, the overall impact of such use is likely to exacerbate and maintain both conditions.

Consistent with the extant literature demonstrating greater suicide risk associated with PTSD and substance use disorder comorbidity (Dore, Mills, Murray, Teesson, & Farrugia, 2011), methamphetamine users with PTSD were more likely to have attempted suicide in their lifetime. These findings are also consistent with recent studies supporting an association between anxiety disorders and suicidality (e.g., Sareen, Houlahan, Cox, & Asmundson, 2005), evidence of higher rates of PTSD and alcohol problems related to greater suicide risk (Pietrzak et al., 2011), and finally, elevated risk of suicide among those who use substances to self-medicate symptoms of PTSD (Leeies, Pagura, Sareen, & Bolton, 2010).

Findings from the current investigation underscore the importance of identifying and addressing PTSD among methamphetamine users seeking treatment. PTSD has been found to be under-recognized in addiction treatment settings, as patients tend not to report traumatic experiences and related symptomatology spontaneously. In these settings, systematic screening for PTSD results in a detection rate four times greater than addiction treatment programs that do not screen for trauma (see van Dam et al., 2012). Given the association of PTSD with poorer methamphetamine use outcomes shown in this study, the potential impact of screening methamphetamine users for PTSD is an important clinical implication of the present findings. Likewise, treatment of PTSD is strongly indicated in the context of addiction treatment.

There are several treatment models for comorbid PTSD and substance use disorder, and a number of recent reviews on integrated interventions suggest that the most promising data

are for treatments incorporating an exposure component (see van Dam et al., 2012). One such intervention targeting stimulant users is the Concurrent Treatment of PTSD and Cocaine Dependence Model, a 16-session intervention which integrates prolonged exposure with cognitive behavioral therapy for stimulant dependence. This treatment was recently modified and renamed Concurrent Treatment of PTSD and Substance Use Disorders with Prolonged Exposure (COPE) (Back et al., 2010). In light of evidence that the response of cocaine versus methamphetamine users to evidenced-based treatments for stimulant use disorders is comparable (Rawson et al., 2000), an important and untested empirical question is whether integrated evidence-based treatments for psychiatrically comorbid cocaine users, such as those with PTSD, also yield comparable outcomes for methamphetamine users. Thus, the COPE model would be a promising treatment to investigate in this regard.

Limitations

Several methodological limitations of this investigation warrant comment. First, the small subgroup of methamphetamine users who met criteria for PTSD limits the power to detect group differences as well as the potential generalizability of the observed effects. In future studies with a larger PTSD subgroup, additional fully-powered analyses can be undertaken to better characterize the relationship between PTSD symptom clusters and methamphetamine use (e.g., evaluation of the association of individual symptoms comprising the clusters with outcomes). Furthermore, the PTSD symptom clusters are not independent of one another; because the clusters are intercorrelated, the unique contribution of each grouping to the variance in outcome is not fully elucidated in this study. Second, the MINI diagnostic interview was performed 3-years post-treatment, and information was not collected to determine the order of onset of PTSD versus methamphetamine dependence. This limits the ability to characterize the effects of treatment on PTSD and to draw definitive conclusions concerning the self-medication hypothesis and other aspects of the relationship between PTSD and post-treatment methamphetamine use (and vice versa). Additionally, the correlational nature of several analyses undertaken precludes causal inferences concerning the association between PTSD and methamphetamine use; as such, prospective studies are warranted to further examine causality between these conditions. Finally, given that participants with severe Axis I disorders requiring hospitalization were excluded from the original study, the generalizability of the follow-up findings is limited to methamphetamine users with moderate psychopathology and symptomatology. Further research is needed to elucidate the temporal relationship of PTSD to methamphetamine dependence and the clinical courses of both conditions.

Acknowledgments

The authors would like to thank the treatment and research staff at the participating community-based center sites, as well as acknowledge the support of the study investigators in each region. The research presented in this paper was supported by NIDA Grant 1K23DA020085 awarded to S. Glasner-Edwards and by the Methamphetamine Abuse Treatment – Special Studies (MAT-SS) contract 270-01-7089 and grants numbers TI 11440–01, TI 11427–01, TI 11425–01, TI 11443–01, TI 11484–01, TI 11441–01, TI 11410–01 and TI 11411–01, provided by the Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA), US Department of Heath and Human Services. The opinions expressed in this publication are solely those of the authors and do not reflect the opinions of the government.

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Table 1

Sample Characteristics (*N*=526)

Characteristic	***n***	**%**
Gender, Male	210	39.9
Race/Ethnicity		
Caucasian	362	68.8
African-American	9	1.7
Hispanic	74	14.1
Asian/Pacific Islander	61	11.6
Other	20	3.8
Marital Status		
Married	119	22.6
Divorced/Separated	190	36.1
Never Married	217	41.3
Employed	316	60.1
Route of Administration		
Smoke	331	62.9
Intranasal	49	9.3
Intravenous	143	27.2
	M	*SD*
Age at Admission	36.2	8.0
Years of Education	12.3	1.7
Number of days using MA, past 30	11.9	9.6

Note: MA = methamphetamine