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Patterns of Methamphetamine Use and Symptoms of Depression Among Young Adults in Northern Thailand

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Abstract

Introduction—Depression often co-occurs with amphetamine type stimulant use and can negatively impact drug treatment outcomes. Understanding the temporal relationship between depressive symptoms and methamphetamine use can further inform both treatment and mental health options.

Methods—Methamphetamine users aged 18 to 25 years were enrolled in a 12-month randomized behavioral trial in Thailand. Questionnaires were administered every three months and included information on substance use and depressive symptoms. Pattern of methamphetamine use during follow-up was characterized into four groups: early cessation, late cessation, relapse and persistent use. Multinomial logistic regression was used to determine the impact of baseline depressive symptoms (CES-D score and % ≥ 22) on patterns of methamphetamine use during follow-up. Linear and logistic regression was used to determine the impact of patterns of methamphetamine use on depressive symptoms at the end of the trial.

Results—No association was found between baseline depressive symptoms and subsequent patterns of methamphetamine use. A significant relationship was found between patterns of methamphetamine use and ensuing depressive symptoms, with those achieving cessation experiencing lower levels of depressive symptoms.

Discussion—Many symptoms of depression may resolve with cessation or reduction in methamphetamine use. Clinical and community-based efforts that facilitate drug users' attempts to stop using drugs should be supported as they may contribute to positive cessation outcomes and help to improve overall mental health.

Keywords

methamphetamine; depression; comorbidity

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1. Introduction

Methamphetamine (MA) use is associated with many health-related harms, including depression (Darke et al., 2008). The prevalence of depression among MA users is higher than the general population, with the majority of MA users reporting a lifetime history of depression (Hall et al., 1996; Zweben et al., 2004) and over a third reporting a lifetime diagnosis of depression (Darke et al., 2008). Cessation of MA use is also associated with symptoms of depression as depression is a major component of the withdrawal syndrome (Markou et al., 2002; McGregor et al., 2005).

The temporal relationship between depression and MA use is unclear, as it is unknown whether experiencing depressive symptoms promotes MA use, whether depression results from or is enhanced by MA use, or whether it is bidirectional. Addressing this issue is clinically relevant as it may inform treatment options for both MA dependence and mental health. Few studies have specifically examined this issue (Peck et al., 2005), however drug treatment studies provide some insight. Antidepressants have been explored as pharmacological agents for the treatment of drug dependence. However, they have not consistently been shown to improve either drug cessation or depressive symptoms among cocaine users (Weddington et al., 1991; Arndt et al., 1992; Kosten et al., 1992; Galloway et al., 1994; Covi et al., 1995; Grabowski et al., 1995; Margolin et al., 1995; Nunes et al., 1995), even among participants with depression (Ziedonis et al., 1991; Margolin et al., 1995; Nunes et al., 1995; Cornelius et al., 1998; Nunes et al., 1998; Schmitz et al., 2001; McDowell et al., 2005), and have mainly been shown to be ineffective among MA users (Galloway et al., 1996; Shoptaw et al., 2006; Elkashef et al., 2008). In contrast, the majority of treatment studies for MA dependence with other pharmacological or behavioral interventions have found an improvement in depressive symptoms after cessation of MA use (Rawson et al., 2002; Baker et al., 2005; Peck et al., 2005; Heinzerling et al., 2006; Shoptaw et al., 2006; Jaffe et al., 2007). The results of these studies suggest that a reduction in MA use can impact psychological distress in terms of depressive symptoms, but the impact of depression on MA cessation remains unclear.

All of these studies have been conducted in the United States among small numbers of treatment-seeking MA users. No studies have yet explored this issue in an international environment outside of the clinical setting. Thailand has experienced an epidemic rise in MA use, particularly among adolescents and young adults (UNODC, 2004), and this group has been found to have a high burden of depressive symptoms (Celentano et al., 2008). We examined the temporal relationship between long-term pattern of MA use and depressive symptoms in the context of a randomized behavioral trial to reduce the harms associated with drug use among non-treatment-seeking young MA users in northern Thailand.

2. Methods

2.1. Study Population

This study was conducted within a 12-month randomized behavioral trial in Chiang Mai, Thailand that aimed to reduce the harms associated with MA use. The trial compared the efficacy of a peer-educator, network-oriented intervention with a best practice, individually-focused life skills curriculum. Between April 2005 and June 2006, 1263 young adults aged 18–25 years were screened, of whom 1189 were eligible (94%) and 983 (78%) were randomized (415 index participants and 568 members of their drug and/or sexual networks). Recruitment procedures and eligibility criteria have been described in detail elsewhere (Celentano et al., 2008). Reasons for ineligibility and non-randomization were primarily related to the index participants' inability to enroll one of their drug or sexual network members into the trial within the specified window of time. After randomization, participants returned at 3, 6, 9, and 12 months for study visits. By the 12-month study visit, 882 (90% of those

randomized) participants remained in the trial. The trial was approved by the Institutional Review Board (IRB) at Johns Hopkins Bloomberg School of Public Health, the Human Experimentation Committee at the Research Institute for Health Sciences, Chiang Mai University, and the IRB of the Ministry of Public Health in Thailand.

This analytic sample consists of 863 participants who reported using MA in the three months prior to baseline (23 excluded) and who returned for at least three follow-up visits (97 excluded). The subset of participants in this analysis did not differ from those excluded on any relevant characteristics at baseline.

2.2. Data Collection

Questionnaires were administered to participants at baseline and each follow-up visit. The questionnaires collected information on sociodemographic characteristics, substance use, depressive symptoms, sexual behaviors and history of incarceration. The substance use section of the questionnaire was based on the widely used Risk Behavior Assessment (Needle et al., 1995) and was modified based on formative research conducted prior to the study (German et al., 2006).

2.3. Measures

Symptoms of depression were measured using the Center for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977). The CES-D contains 20 items that measure self-reported symptoms of depression. Participants reported the frequency of experiencing each item in the previous week on a scale from 0 (rarely or none of the time) to 3 (most or all of the time). Items were summed to obtain a score ranging from 0 to 60. A cutoff of ≥ 22 was used to define high levels of depressive symptoms, as recommended following validation of the CES-D scale in Thailand (Trangkasombat et al., 1997).

A participant's pattern of MA use was defined based on self-reported MA use in the three months prior to each study visit. All participants reported using MA in the three months prior to baseline and were required to have attended at least three follow-up visits. Four patterns were defined, based on previous research among illicit drug users (Galai et al., 2003): early cessation, late cessation, relapse, and persistence (Figure 1). Early cessation was defined as reporting no use of MA at any visit after baseline. Late cessation was defined as reporting use at baseline and one or more subsequent follow-up visits and then reporting no use of MA until the end of the trial. Relapse was defined as transitioning from no use to use of MA in two consecutive visits at any point during follow-up. Persistence was defined as reporting use of MA at all follow-up visits after baseline. Behaviors were carried forward for participants with missing visits (4% of participants).

Potential confounders included gender, education, intervention condition as randomized, baseline depressive symptoms (CES-D score and CES-D ≥ 22), measures of alcohol use at last visit (frequency of alcohol use, frequency of drunkenness, or CAGE score (Ewing, 1984)), frequency of MA use at baseline (once a week or less and more than once a week), and the use of illicit drugs other than MA in the three months prior to the last visit.

2.4. Statistical Analysis

Mean differences in CES-D score between the baseline and last follow-up visit were evaluated using paired t-tests for each MA group.

To investigate the relationship between depressive symptoms and future MA use, mean CES-D score and the proportion with high levels of depressive symptoms at baseline were compared between the four groups of MA users using Analysis of Variance (ANOVA) and chi-squared

tests, respectively. To take into account potential confounders, multinomial logistic regression was used with depressive symptoms as either a linear (CES-D score) or binary ($\text{CES-D} \geq 22$) exposure.

To investigate the relationship between MA use and future symptoms of depression, mean CES-D score and the proportion with high levels of depressive symptoms at the last visit (either the nine- or 12-month follow-up visit) were compared between the four groups of MA users using ANOVA and chi-squared tests, respectively. To take into account potential confounders, linear regression was used to model CES-D score and logistic regression was used to model $\text{CES-D} \geq 22$. Interactions by gender, use of other drugs and frequency of MA use at baseline were explored. All analyses were conducted using SAS for Windows Version 9.1 (SAS Institute Inc., Cary, NC).

Forty-two percent of participants used drugs other than MA during the trial (primarily marijuana), which may have affected their level of depressive symptoms as well as their ability to cease using MA. A sensitivity analysis was performed, restricting the study population to participants who did not report use of other drugs during follow-up. Levels of depressive symptoms were slightly lower among this subgroup, however similar results were found for both depressive symptoms at baseline and last study visit by patterns of MA use during follow-up (data not shown).

3. Results

Characteristics of the study population are presented in Table 1. The study population was predominantly male (73%), younger than 20 years of age (28%), ethnically Thai (99%) and Buddhist (97%). Most participants had a current girlfriend or boyfriend (78%) and 40% were still in school at baseline. Alcohol use was common, with 51% reporting drinking four or more days a week and 75% had a CAGE score indicative of alcohol dependence. All participants reported using MA at baseline, with the majority (63%) using at least once a week. Use of illicit drugs other than MA, primarily marijuana, was also common (79%), and more than half (56%) reported ever having sold or delivered drugs.

MA use declined during follow-up, with only 55% of participants reporting use in the prior three months by the end of the trial. Fifteen percent of all participants ceased using MA after baseline and made up the early cessation group, 24% ceased using MA at a later study visit and made up the late cessation group, and 24% made up the relapse group. Thirty-seven percent of participants reported using MA at all of their study visits, and they comprised the persistence group. There were significant differences between the four groups with regards to demographics and substance use (Table 1). Participants who ceased using MA were more likely to be female, have completed high school, currently be in school, use MA at a lower frequency, have started using MA at a later age, and they were less likely to have a history of using drugs other than MA and selling or delivering drugs. Only 42% of participants used drugs other than MA (primarily marijuana) during follow-up, with significant differences between the four groups (early: 21%; late: 38%; relapse: 40%; persistent: 54%; $p < 0.0001$). Among those in the late cessation group, almost 90% of participants reported no use of other drugs by the end of the study.

Symptoms of depression at baseline were common in this population, with a mean CES-D score of 18.3 (SD: 9.1) and 35% reported high levels of depressive symptoms (Table 2). Mean CES-D scores and the prevalence of high levels of depressive symptoms declined during the trial to a mean of 16.7 (SD: 9.4) and prevalence of 31% at 12 months, respectively.

In the analysis of baseline depressive symptoms and subsequent pattern of MA use, no significant differences were found (Table 2) for either the mean CES-D score or the prevalence

of high levels of depressive symptoms, even after adjusting for potential confounders (data not shown). In contrast, significant differences were found in both mean CES-D score and the prevalence of high levels of depressive symptoms at the last visit by pattern of MA use during follow-up, as a result of significant reductions in CES-D score from baseline in the early cessation (mean decrease of 2.2 points; SD: 10.0), late cessation (3.4; SD: 9.5) and relapse groups (1.7; SD: 9.0), but not in the persistence group (0.2; SD: 10.0) (Figure 2). At the last visit, mean CES-D scores and the odds of high levels of depressive symptoms were significantly lower in the early and late cessation groups as compared to the persistence group (Table 3). Mean CES-D scores did not differ significantly between the early and late cessation groups. Both measures of depressive symptoms were lower in the relapse group as compared to the persistence group; however the results were only marginally significant. Similar results were obtained after adjusting for potential confounders.

A marginally significant interaction ($p < 0.10$) by frequency of baseline MA use was found in the relationship between pattern of MA use and depressive symptoms at last visit, potentially indicating that participants who used MA more frequently at baseline (two or more times per week) and were able to reduce/cease their use of MA had greater decreases in CES-D scores from baseline than participants who used at a lower frequency.

4. Discussion

In this study of MA users, co-occurrence of high levels of depressive symptoms was common and the frequency of both depressive symptoms and MA use declined during the trial. We found that baseline depressive symptoms did not predict subsequent patterns of MA use over the 12 months of follow-up, but rather that patterns of MA use predicted levels of depressive symptoms at the end of follow-up. Four distinct groups of MA users were identified by their long-term pattern of drug use over 12 months. A large proportion of participants were able to stop using MA, as well as other drugs, for a period of time and they evidenced significantly fewer depressive symptoms than participants who continued to use MA, with no apparent difference by the timing of cessation (early vs. late). Despite intermittent use of MA in the relapse group, these participants also had fewer depressive symptoms, although to a lesser extent than those able to sustain cessation. These findings provide evidence of a temporal relationship between MA cessation and depressive symptoms,

To our knowledge, the only other study to evaluate the temporal relationship between depressive symptoms and MA use was conducted among gay and bisexual treatment-seeking men in the U.S. (Peck et al., 2005). This study supports the findings of these authors and substantially broadens the reference population. Support for this relationship also comes from studies of the impact of depression on treatment for alcohol and drug dependence. The results of these studies have been inconsistent, with some studies predicting poorer treatment outcomes among depressed participants (Rounsaville et al., 1982; McLellan et al., 1986; Rounsaville et al., 1986; Greenfield et al., 1998; McKay et al., 2002; Hasin et al., 2004), and others finding no association (Booth et al., 1991; Miller et al., 1996; Sellman et al., 1996; Brown et al., 1998). The use of antidepressants for treatment of MA dependence have also not found to be effective in reducing MA use despite decreases in depressive symptoms (Galloway et al., 1996; Shoptaw et al., 2006; Elkashef et al., 2008). In contrast, studies evaluating cessation or reductions in MA use, as well as other substances, after treatment have consistently reported improvements in depressive symptoms following reductions in drug use (Rawson et al., 2002; Nunes et al., 2004; Baker et al., 2005; Peck et al., 2005; Heinzerling et al., 2006; Shoptaw et al., 2006; Jaffe et al., 2007). Given the pervasive co-occurrence of drug use and depression (Grant et al., 2004) these findings suggest that providing assistance for MA cessation may help to address concomitant mental health burdens.

Most studies of MA and depression have been conducted within the context of treatment trials among participants seeking treatment and may therefore represent a less diverse population of drug users than would be found in a community sample. It is possible that the treatment-based samples were skewed to higher levels of use, making it difficult to determine whether associations between cessation and depressive symptoms would be found among populations using at a lower frequency. In this study, participants were not seeking treatment and a high degree of variation in frequency of use was found. The consistency of the findings indicates that cessation contributes to reduced depressive symptoms independent of any particular treatment modality, even among a diverse sample. The diversity of the study population also allowed for differences by the frequency of MA use at baseline to be evaluated. A marginally significant interaction was found, with greater decreases in depressive symptoms among participants using at a higher frequency at baseline who were able to reduce use during follow-up. More research is needed in community-based samples to explore this finding. It may be an indication of the physiological response to reduced MA consumption or may indicate differing evaluations of cessation among lower frequency users.

There are several limitations that should be considered when interpreting the results of this study. First, the CES-D scale only measures depressive symptoms in the week prior to the study visit, and therefore cannot capture symptoms experienced outside of this window of time. This limitation was diminished by the relatively frequent study visits, however, rates of depressive symptoms may have been underestimated using this measure. Second, the determination of pattern of MA cessation was based on a relatively short follow-up duration (one year), and it is unknown whether these patterns persisted after the end of the trial. To minimize this concern and most accurately characterize use, the analysis was restricted to participants with four or more study visits. Third, this study was conducted in the context of a trial, therefore the study design and eligibility criteria may have influenced the observed patterns of MA use. Fourth, this study looked only at distinct patterns of MA use during follow-up and their relationship with depressive symptoms and therefore did not consider the short-term effects that each may have on the other. Lastly, clinical histories of depression and the timing of onset of depressive symptoms in relation to substance use were not available. Consequently, distinctions between primary and substance-induced depressive symptoms could not be made in this study and their respective relationships with MA use and cessation could not be examined.

Despite these limitations, the findings from this study add to the body of research in this area and support integrated treatment approaches that consider both the patient's mental health and substance use in determining the optimal treatment plan. Whether independent or substance-induced, depressive symptoms improved significantly among participants who achieved cessation by the end of the trial, a desirable outcome given the potential impact of both types of symptoms on future episodes of depression (Nunes et al., 2006) and the negative impact of depressive symptoms during periods of abstinence on the risk of relapse into dependence (Hasin et al., 2002). Clinical and community-based efforts that facilitate drug users' attempts to stop using drugs should be supported. These efforts may contribute to positive cessation outcomes and help to improve overall mental health..

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A. EARLY CESSATION **B. LATE CESSATION** **C. RELAPSE** **D. PERSISTENCE**

Figure 1.
 Characterization of MA use patterns during follow-up by reported MA use in the three months prior to each study visit

Figure 2. Mean CES-D score over time by pattern of methamphetamine use during follow-up among young adults in northern Thailand

Note: CES-D denotes the Center for Epidemiological Studies Depression Scale(Radloff, 1977)

Table 1
Baseline characteristics of young methamphetamine users in northern Thailand

	Total Population (n=863) N (%)	Early Cessation (n=132) N (%)	Late Cessation (n=209) N (%)	Relapse (n=202) N (%)	Persistence (n=320) N (%)
Male gender [†]	631 (73.1)	84 (63.6)	149 (71.2)	150 (74.3)	248 (77.5)
Age > 20 years	278 (32.2)	43 (32.6)	59 (28.3)	58 (28.7)	118 (36.9)
Religion – Buddhist	838 (97.1)	129 (97.7)	203 (97.1)	195 (96.5)	311 (97.2)
Ethnicity – Thai	858 (99.4)	132 (100.0)	208 (99.5)	199 (98.5)	319 (99.7)
Current girlfriend/boyfriend	676 (78.3)	106 (80.3)	165 (79.0)	157 (77.7)	248 (77.5)
Completed High school [†]	161 (18.7)	37 (28.0)	41 (19.6)	38 (18.8)	45 (14.1)
Employment status [†]					
Student	342 (39.6)	63 (47.7)	99 (47.4)	81 (40.1)	99 (30.9)
Employed	321 (37.2)	39 (29.6)	67 (32.1)	77 (38.1)	138 (43.1)
Unemployed	200 (23.2)	30 (22.7)	43 (20.6)	44 (21.8)	83 (25.9)
Frequency of alcohol use					
≤1 day a week	147 (17.0)	29 (22.0)	37 (17.7)	32 (15.8)	49 (15.3)
2–7 days a week	716 (83.0)	103 (78.0)	172 (82.3)	170 (84.2)	271 (84.7)
CAGE score ≥ 2	645 (74.7)	106 (80.3)	151 (72.3)	150 (74.3)	238 (74.4)
Frequency of MA use [†]					
≤1 day a week	430 (49.8)	92 (69.7)	106 (50.7)	101 (50.0)	131 (40.9)
2–7 days a week	433 (50.2)	45 (34.1)	103 (49.3)	101 (50.0)	189 (59.1)
Route of MA administration: smoking	860 (99.7)	130 (98.5)	208 (99.5)	202 (100.0)	320 (100.0)
Age of first MA use ≤ 15 yrs [†]	540 (62.6)	56 (42.4)	119 (56.9)	139 (68.8)	226 (70.6)
Lifetime use of other drugs [†]					
MA only	188 (21.8)	42 (31.8)	53 (25.4)	35 (17.3)	58 (18.1)
MA and ≥ 1 other drug	675 (78.2)	90 (68.2)	156 (74.6)	167 (82.7)	262 (81.9)
History of selling or delivering drugs [†]	487 (56.4)	55 (41.7)	102 (48.8)	120 (59.4)	210 (65.6)

[†] p<0.05 for difference between groups

MA: methamphetamine

Table 2

Depressive symptoms at baseline and last visit by pattern of methamphetamine use among young adults in northern Thailand

Pattern of Methamphetamine Use Over Follow-Up	Baseline Depressive Symptoms		Depressive Symptoms at Last Visit	
	Mean CESD (SD)	CESD $\geq$ 22 N (%)	Mean CESD (SD)	CESD $\geq$ 22 N (%)
Early cessation (n=132)	17.5 (8.6)	42 (31.8)	15.2 (9.3)	29 (22.0)
Late cessation (n=209)	18.7 (9.2)	69 (33.0)	15.3 (9.2)	55 (26.3)
Relapse (n=202)	18.5 (9.5)	76 (37.6)	16.8 (9.6)	62 (30.7)
Persistence (n=320)	18.4 (8.9)	118 (36.9)	18.1 (9.3) [†]	119 (37.2) ^{†‡}
Total (n=863)	18.3 (9.1)	305 (35.3)	16.7 (9.4)	265 (30.7)

[†] p<0.05 for differences by pattern of methamphetamine use

[‡] p<0.05 for test for trend

Note: CES-D denotes the Center for Epidemiological Studies Depression Scale(Radloff 1977)

Table 3

Difference in mean CES-D score and odds ratios for high levels of depressive symptoms at last visit by pattern of methamphetamine use among young adults in northern Thailand

Pattern of Methamphetamine Use Over Follow-Up	Difference in Mean CES-D Score		Odds Ratios for High Levels of Depressive Symptoms (CES-D $\geq$ 22)	
	Crude Mean (SE)	Adjusted* Mean (SE)	Crude OR (95% CI)	Adjusted* OR (95% CI)
Early cessation (n=132)	-2.87 (0.97) [†]	-2.36 (0.89) [†]	0.48 (0.30, 0.76)	0.44 (0.26, 0.74)
Late cessation (n=209)	-2.86 (0.83) [†]	-2.46 (0.75) [†]	0.60 (0.41, 0.88)	0.66 (0.43, 1.00)
Relapse (n=202)	-1.35 (0.84)	-1.42 (0.74)	0.75 (0.51, 1.09)	0.68 (0.46, 1.03)
Persistence (n=320)	Ref.	Ref.	Ref.	Ref.

* Adjusted for gender, education, baseline CESD/high levels of depressive symptoms, intervention arm, frequency of drunkenness at last visit, frequency of methamphetamine use at baseline, use of other drugs in the 3 months prior to the last visit

[†] p<0.05

Note: CES-D denotes the Center for Epidemiological Studies Depression Scale(Radloff 1977)