

Implicit Attitudes and Addictive Behaviors Among Methamphetamine Users: The Moderation of Depression

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Introduction: Methamphetamine use disorder is a major mental health issue worldwide. An implicit attitude is a potential way to understand the paradoxical behavior of substance use and has not been fully investigated for methamphetamine users. Depression is a common comorbidity for methamphetamine users. Little is known about the moderating effects of depression on the associations between implicit attitudes and addictive behavior in methamphetamine users. The aims of this study were to examine the associations of implicit attitudes with methamphetamine-dependent behavior and the moderation of depression in these associations.

Methods: One-hundred and fifty methamphetamine users were enrolled. Epidemiological data, methamphetamine dependence severity, and implicit attitudes were collected.

Results: The results showed that participants have positive implicit attitudes toward methamphetamine and that the implicit attitude is positively related to dependence severity. Depressive methamphetamine users have greater levels of positive implicit attitudes and dependence severity. Furthermore, depression positively moderates the relationships between implicit attitudes and use behavior.

Conclusion: These results highlight the importance of implicit attitudes and depression for methamphetamine dependence and indicate that depression can strengthen the relationship between implicit attitudes and methamphetamine-use behavior. Therefore, both implicit attitudes and depression are areas to be addressed in the treatment of methamphetamine use disorder.

Keywords: implicit attitude, dependence, methamphetamine, moderation and depression

Introduction

Methamphetamine is reported to be the most common seizure and synthetic stimulant drug used worldwide. The trend of methamphetamine use increased from 2010 to 2020.¹ Methamphetamine use is a major health issue worldwide, particularly in North America and Southeast Asia. In Taiwan, the study has shown that methamphetamine is not only one of the most frequently used illicit drugs, but also one of the most addictive drugs.² In addition, methamphetamine use is usually comorbid with physical illnesses, such as HIV, and mental illnesses, such as psychotic disorders or depression.³ Due to the increased addictive propensity and rate of use and comorbidities, exploring psychopathy related to methamphetamine use is an unmet need.

A central paradox of substance use behavior is that 1) substance users consume continually even when they are aware of the negative consequences and 2) substance use behavior can be triggered spontaneously.^{4,5} The dual processes model postulates two processes underlying behavior: an explicit and controlled process and an implicit and automatic process.⁶ Unlike explicit cognitive approaches to substance use behavior, which assume that individuals weigh the pros and cons in a reflective way to decide, implicit cognition assumes that the automatic action tendency may drive behavior without conscious control. Therefore, implicit cognitions have become increasingly recognized in the context of substance use behavior and can help to explain the paradoxical behavior of substance use.⁵

Traditionally, assessments of individuals with substance use disorders are based on information provided by individuals themselves during interviews. Most of this information is a product of consciousness and is easily influenced by patients' intentions or social desirability biases. This is a potential limitation for understanding substance use behavior. In contrast, evaluations of implicit cognition rely on tests that do not require conscious or deliberate recollection of previous events or introspections about the causal attributions of behavior. Therefore, implicit cognition may provide less subjective information for our understanding of substance use behavior.

A previous study showed that implicit attitude, a process of implicit cognition and an indicator for automatic action tendency, may reliably predict substance use behavior.⁷ There is limited evidence on the relationship between implicit attitudes and methamphetamine-dependent behavior. Several indirect methods are available that assess implicit attitudes and provide hints about implicit processes. The Implicit Association Test (IAT) proposed by Greenwald et al is an indirect assessment used to interrogate implicit attitudes which can be an indicator for automatic action tendencies.^{8,9} The IAT has successfully been used to investigate substance use behavior and has increasingly been used to study the cognitive mechanisms that underlie drug craving and use behavior.⁷ Therefore, using the IAT to evaluate the implicit attitudes of methamphetamine users can provide a better understanding of how implicit cognition relates to methamphetamine-dependent behaviors.

Phelps et al reported that the level of implicit attitude is linked to amygdala activation.¹⁰ Stanley and colleagues reviewed previous research and concluded that the amygdala is the brain region that contributes to the expression of implicit attitudes.¹¹ In addition, lesion mapping research has shown that the dorsolateral prefrontal cortex (DLPFC) has a causal contribution to the effect of implicit attitude, which is measured by the IAT, on explicit behavior.¹² Depression is a common comorbidity for substance users and is associated with poor treatment outcomes and increased suicide risk.³ The level of depression is related to the activities of the amygdala and DLPFC.¹³ Therefore, depression may modify implicit attitude expression because both depression and implicit attitude are related to the amygdala and DLPFC. In addition, Wiers et al proposed that the ability of the automatic implicit approach process to engage in substance dependence severity can be moderated by emotion.¹⁴ However, due to the high comorbidity rate of depression among people using methamphetamine, few studies have examined the moderating effect of depression on the association between implicit attitudes and substance use behavior.

This study aimed to examine the associations of methamphetamine craving and dependence severity with implicit methamphetamine attitudes and to explore the effects of depression on the associations between implicit methamphetamine attitudes and craving and dependence severity in methamphetamine users. We hypothesized that the implicit attitude toward methamphetamine would exhibit significantly positive associations with craving and methamphetamine dependence severity. We also hypothesized that methamphetamine users with depression would show a significantly stronger implicit attitude toward methamphetamine than those without depression and that depression can moderate the association between implicit methamphetamine attitudes and dependence-related behavior.

Methods

Participants

Methamphetamine users were recruited from hospital-based outpatient services. The inclusion criteria for the present study were (1) diagnosis of methamphetamine use disorder by psychiatrists; (2) no comorbid substance use disorder other than tobacco; (3) no psychiatric diagnosis of schizophrenia or bipolar disorder; and (4) no major physical disease. Initially, all participants who did not receive any drug intervention were interviewed by psychiatrists to assess whether they had methamphetamine use disorder or not and fulfilled the other inclusion criteria. If they met the inclusion criteria, then the researchers explained the present study to them. Written informed consent was obtained if the patients agreed to participate in the study. The presented study complied with the Declaration of Helsinki and the Institutional Review Board of Kaohsiung Medical University reviewed and approved this study (KMUHIRB-SV(II)-20170072). The participants underwent interviews to collect epidemiology and methamphetamine-related data, including age, sex, level of education, and current methamphetamine use.

Assessment

Visual Analog Craving Scale (VACS)

The modified VACS, which was adopted from previous studies, was used to evaluate the level of craving for methamphetamine in individuals with methamphetamine use disorder.¹⁵ The VACS is composed of the following single question: how much did you crave/desire/want to use methamphetamine in the preceding week? The intensity of craving was rated from 0 (not at all) to 100 (very much).

Chinese-Mandarin Version of the Severity of Dependence Scale (SDSch)

The SDS^{ch}, which is composed of 5 questions, was used to assess the severity of dependence on methamphetamine in the preceding week.¹⁶ The range of the score on the SDS^{ch} is from 0 to 15. A higher score indicates greater dependence severity.

Chinese Version of the Center for Epidemiological Studies-Depression Scale (CES-Dch)

The CES-D^{ch} is a 20-item measure for assessing the severity of depressive symptoms and has been validated among Taiwanese adults in the community.¹⁷ Subjects were asked how often they had encountered each symptom during the past week. The response options ranged from 0 to 3 (0= rarely or none of the time (less than 1 day), 1= some or a little of the time (1-2 days), 2= occasionally or a moderate amount of the time (3-4 days), or 3= most or all of the time (5-7 days)). The scores on these response options were reversed for the four negatively worded items. Scores range from 0 to 60, with a higher CES-D total score indicating a greater level of depression. The cutoff score for depression was 16.

Computerized Implicit Association Test (IAT) for Methamphetamine

The level of implicit attitudes toward methamphetamine was evaluated by the IAT. In presenting the IAT to the participants, we followed the procedure described by Greenwald.¹⁸ The target discrimination is methamphetamine-related cues vs neutral cues, and the attribute discrimination is pleasure vs aversion. We used approach vs avoid as attribute labels because these categories are strongly associated with inner motivation. The stimulus material consisted of 6 methamphetamine-related cues (pictures) and 6 neutral cues (pictures) as well as 6 approach and 6 avoid words. Phase 1 consisted of 24 trials in which methamphetamine-related and neutral pictures were presented. During Phase 2, approach and avoid words were presented in 24 trials. Phase 3 consisted of two blocks of 48 trials, during which each word or picture was presented twice. The approach word and methamphetamine-related pictures were classified to the left side in the 48 trials. Phase 4 was identical to phase 1, except that the methamphetamine-related pictures were classified to the right side and neutral pictures were classified to the left side. Phase 5 consisted of two blocks of 48 trials, during which each word or picture was presented twice. The approach words and neutral pictures were classified to the left side in the 48 trials. The IAT score was calculated as the difference in score between the mean response times of the methamphetamine-approach/neutral-avoidance block and the neutral-approach/methamphetamine-avoidance block, with larger scores indicating stronger automatic approach motivation toward methamphetamine. The IAT score was calculated according to the D-measure algorithm suggested by Greenwald.¹⁸

Data Analysis

The epidemiological and methamphetamine-related characteristics were presented by descriptive analysis. The comparisons of methamphetamine-related characteristics between groups were analyzed by Student's *t*-test for continuous variables and the chi-square (χ^2) test for categorical variables. Pearson's correlation was used to explore the relationships between implicit attitudes and methamphetamine-related characteristics. Analysis of covariance (ANCOVA) was applied to examine associations between implicit attitudes and depression and between methamphetamine-related characteristics and the effects of age, gender, education, age of start of methamphetamine use, and duration of methamphetamine use.

A moderation model was used to explore whether depression was a moderator of the relationship between implicit attitudes and methamphetamine-related behavior. The sequential Bonferroni procedure was used to adjust for multiple comparisons.

Results

The Epidemiology, Methamphetamine-Related Characteristics and Depression of All Participants

The present study enrolled one-hundred and fifty individuals with methamphetamine use disorder. Sixteen individuals (10.7%) were female. The mean (SD) age, level of education, age at start of methamphetamine use, and duration of methamphetamine use were 35.58 (9.71), 12.24 (3.01), 25.09 (9.96), and 5.46 (6.76), respectively. The percentage of females did not significantly differ between non-current and current methamphetamine group (non-current group: 9.26%; current group: 14.29%, $\chi^2 = 0.802$, $p = 0.371$). The difference of rates of females between non-depressive and depressive group was not significant (9.68% vs 11.36%, $\chi^2 = 0.109$, $p = 0.742$). The results of the IAT showed that there was a positive implicit attitude toward methamphetamine (mean = 0.58, SD = 0.68). In addition, implicit attitudes were significantly more positive for current methamphetamine users than for non-current methamphetamine users (Table 1). The rate of depression for participants was 41.3%. The depressed methamphetamine users showed significantly greater levels of craving, implicit attitudes toward methamphetamine, and severity of methamphetamine dependence (Table 2). In addition, current methamphetamine users had significantly greater rates of depression than non-current users (66.67% vs 31.48, $\chi^2 = 15.439$, $p < 0.001$).

Relationships of Implicit Attitudes Toward Methamphetamine with Epidemiological and Methamphetamine Use-Related Characteristics

The associations of implicit attitude with depression and craving severity and severity of dependence were significant (Pearson's correlation for depression = 0.32, $p \leq 0.001$; Pearson's correlation for craving = 0.54, $p \leq 0.001$; Pearson's correlation for severity of dependence = 0.50, $p \leq 0.001$). The level of implicit attitude did not significantly differ by gender and was not related to age, education level, age at start of methamphetamine use or duration of methamphetamine

Table 1 Comparisons of Enrolled Individuals with and without Current Methamphetamine Use

	Non-Current Users (n=108)	Current Users (n=42)	p
Age at start of methamphetamine use (years)	25.85 (10.52)	23.14 (8.14)	0.135
Duration of methamphetamine use (years)	5.19 (6.84)	6.16 (6.55)	0.429
Level of craving ^a	46.60 (24.22)	61.43 (23.33)	0.001
Level of implicit attitude ^b	0.45 (0.61)	0.92 (0.74)	0.001
Level of methamphetamine dependence ^c	6.56 (3.38)	8.74 (3.52)	< 0.001

Notes: a: measured by VAS; b: measured by IAT; c: measured by SDS.

Table 2 Comparisons of Craving, Level of Methamphetamine Dependence, Methamphetamine Use and Implicit Attitude Between Depressive and Non-Depressive Individuals with Methamphetamine Use Disorder

	Depressive (n=62) Mean (SD) or N (%)	Non-Depressive (n=88) Mean (SD) or N (%)	p
Level of craving ^a	61.61 (22.34)	42.61 (23.61)	< 0.001
Level of implicit attitude ^b	0.82 (0.68)	0.42 (0.63)	< 0.001
Level of methamphetamine dependence ^c	8.48 (3.30)	6.24 (3.43)	< 0.001
Current methamphetamine use			< 0.001
No	34 (54.84)	74 (84.09)	
Yes	28 (45.16)	14 (15.91)	

Notes: a: measured by VAS; b: measured by IAT; c: measured by SDS.

use. Depression severity was significantly related to age at the start of methamphetamine use, level of craving and severity of dependence (Pearson's correlation for age at the start of methamphetamine use = -0.23 , $p \leq 0.001$; Pearson's correlation for craving = 0.40 , $p \leq 0.001$; Pearson's correlation for severity of dependence = 0.28 , $p \leq 0.001$).

Prediction of Depression and Implicit Attitudes Toward Methamphetamine and Craving, Severity of Dependence and Current Methamphetamine Use

The regression analysis showed that after controlling for epidemiological factors, age at the time of use and duration of methamphetamine use, methamphetamine use can predict a greater level of craving and severity of methamphetamine dependence in methamphetamine users (Table 3). Depressive methamphetamine users also showed an increased risk of current methamphetamine use. A higher level of implicit attitudes toward methamphetamine can anticipate a greater level of craving and severity of methamphetamine use after adjusting for the effect of depression. The risk of current methamphetamine use increased as the level of implicit attitude increased.

The interactions between depression and implicit attitudes on craving and severity of dependence were significantly positive when controlling for epidemiological factors, age, and years of methamphetamine use (Table 4). Depression also had a positive moderating effect on the association between the strength of implicit attitudes and current methamphetamine use after we adjusted for the effects of epidemiological factors, age and years of methamphetamine use. The simple effects of implicit attitudes on craving for depressive and non-depressive group were significant (coefficient for

Table 3 The Associations of Implicit Attitude and Depression with Craving, Level of Dependence and Current Amphetamine Use

	Craving ^d		Severity of Dependence ^e		Current Amphetamine Use ^f	
	Coefficient	p	Coefficient	p	Odds Ratio	p
Gender ^a	-6.78	0.215	-0.91	0.265	0.60	0.433
Age (years)	-0.38	0.089	-0.07	0.042	0.94	0.038
Level of education (years)	0.10	0.868	0.07	0.395	1.00	0.992
Age at start of amphetamine use (years)	0.29	0.233	0.03	0.352	1.04	0.311
Duration of amphetamine use (years)	0.07	0.830	-0.003	0.357	1.07	0.133
Depression ^b	12.67	< 0.001	1.42	0.008	3.30	0.005
Level of implicit attitude ^c	18.11	< 0.001	2.36	< 0.001	2.57	0.008

Notes: a: female as reference; b: non-depressive individuals as reference; c: measured by IAT; d: measured by VAS; e: measured by SDS^{ch}; f: non-current use as reference.

Table 4 The Moderating Effects of Depression on Association of Implicit Attitude with Craving, Level of Dependence and Current Amphetamine use. The Moderating Effects of Depression on Association of Implicit Attitude with Craving, Level of Dependence and Current Amphetamine Use

	Craving		Severity of Dependence		Current Amphetamine use	
	Coefficient	p	Coefficient	p	Odds ratio	p
Gender ^a	-5.57	0.284	-0.72	0.350	0.94	0.928
Age (years)	-0.29	0.175	-0.05	0.089	0.94	0.050
Level of education (years)	0.21	0.705	0.09	0.267	1.02	0.841
Age at start of methamphetamine use (years)	0.21	0.352	0.02	0.520	1.03	0.406
Duration of amphetamine use (years)	0.05	0.876	-0.01	0.896	1.07	0.125
Depression ^b	4.05	0.379	0.08	0.902	0.34	0.207
Level of implicit attitude ^c	12.34	< 0.001	1.47	0.002	0.79	0.608
Interaction effect between depression and implicit attitude	13.13	0.007	2.03	0.005	23.70	0.001

Notes: a: female as reference; b: non-depressive individuals as reference; c: measured by IAT.

non-depressive group: 12.34; $p=0.001$; coefficient for depressive group: 24.25; $p<0.001$). The simple effect of implicit attitudes on severity of dependence for depressive and non-depressive group were also significant (coefficient for non-depressive group: 1.47; $p=0.002$; coefficient for depressive group: 3.50; $p<0.001$). The simple effect of implicit attitude on current methamphetamine use is significant for depressive group (odd ratio for non-depressive group: 0.79; $p=0.608$; odd ratio for depressive group: 18.59; $p=0.001$).

Discussion

The present study had several important findings. First, individuals with methamphetamine use disorder have positive implicit attitudes toward methamphetamine. Furthermore, implicit attitudes are more positive for current than for non-current methamphetamine users. Second, more positive implicit attitudes are associated with more craving and a greater severity of dependence. The risk of current methamphetamine use increases as the implicit attitude toward methamphetamine increases. Third, depression can moderate the associations between implicit attitudes and craving and between the severity of dependence and the risk of amphetamine use.

Individuals with methamphetamine use disorder showed a positive implicit attitude toward methamphetamine. Using the IAT, Wildenberg et al conducted a study of heavy alcohol users and found that participants had a positive implicit attitude toward alcohol use.¹⁹ Turel et al conducted a study on implicit attitudes toward the formation and maintenance of excessive social media use among university students. They showed that the level of implicit attitude was positively associated with the use of social media.²⁰ Sherman et al examined implicit attitudes in smokers and showed that smokers have more positive attitudes toward smoking.²¹ Our findings resembled the results of previous studies on substance and non-substance dependencies other than methamphetamine and highlighted the importance of implicit attitudes on substance use behavior.

A prominent conception is that implicit attitudes stem from past experiences.²² A study of smokers that showed that implicit attitudes toward cigarettes were associated with smokers' early experiences supported this idea.²³ Knowledge of the neurobiological substrates of substance use behavior has supported the concept of three temporally sequenced stages of substance use behavior.²⁴ The binge and intoxication stage of substance use is related to the acute rewarding effect of drug use to reinforce drug use.²⁵ This effect of psychostimulant drugs has long been known to be associated with activation of mesolimbic dopamine systems.²⁶ The activation of these systems may result in positive effects on stimulant drug use. In the withdrawal/negative affect stage, a decrease in dopaminergic activity in the mesolimbic system and dysregulation of neurotransmitter systems involved in stress and anxiety-like effects are associated with increased sensitivity to drug use.²⁷ Drug use can reduce withdrawal symptoms, and negative affect also contributes to positive experiences. In the preoccupation stage, craving, the key element of this stage, is associated with drug relapse behavior and implicitly enhances the conditioned reinforcing value.²⁸ All this evidence may support why individuals who use methamphetamine have a positive implicit attitude toward this drug.

The present study revealed that current users have more positive implicit attitudes than non-current users. This finding is in accordance with a previous study showing that smokers have more positive implicit attitudes than abstainers.²⁹ Positive implicit evaluations may contribute to implicit approach tendencies, which may be involved in wanting. Therefore, positive implicit evaluations of substances are assumed to increase the likelihood of approach behavior and use.³⁰ Rooke et al conducted a meta-analysis and showed that implicit cognition is a reliable predictor of substance use.⁷ A previous study also showed that a positive implicit attitude toward cocaine, a CNS stimulant similar to methamphetamine, may be associated with increased use.³¹ Our results indicated that people with more positive implicit attitudes toward methamphetamine are more likely to use methamphetamine. Both results supported the idea that a positive implicit attitude is a risk factor for stimulant use behavior. The formation of implicit attitudes is thought to be a slow process. Once implicit attitudes are formed, they are less possible to change consciously.³² This feature enhances the potential of using implicit attitude as a predictor for stimulant use in individuals with stimulant use disorders.

The present study showed that methamphetamine users with depression have stronger positive implicit attitudes and associations between implicit attitudes and addictive behavior than non-depressive methamphetamine users. Our results were consistent with those of a previous study conducted by Wardell et al, which indicated that negative mood is a moderator in the relationship between implicit attitudes toward alcohol and alcohol consumption.³³ The presence of negative mood can create a cognitive load that reduces the resources available to the executive control system that typically maintains automatic processing, such as implicit associations, and thereby increases the influence of automatic

cognitive processes.³⁴ This is one possible explanation for the findings that negative mood strengthens the relationships between implicit associations and methamphetamine-related outcomes. Another possibility is that depression may increase the activation of implicit cognitions, which may lead to substance use symptoms and behavior.³⁵ This is especially crucial for individuals who use substances to reduce depression, because repeatedly associating substance use with depression reduction may result in stronger implicit cognitive activation during depressive moods.³⁶

The present study also had limitations. First, implicit cognition other than implicit attitudes was not explored in our study. Sally et al reviewed previous studies and showed that other implicit cognitions, for example, attentional bias, may be related to substance use.⁷ This warrants further study to examine the association between implicit cognitions other than implicit attitudes and methamphetamine-related outcomes. Another limitation was the homogeneity of the sample, which consisted of a clinical population. Future research should examine these processes in methamphetamine-treated individuals who do not have access to treatment and in methamphetamine-using offenders in detention centers to extend the generalizability of the findings. Third, as this study was cross-sectional, causal relationships between implicit associations and methamphetamine behaviors cannot be inferred. Longitudinal studies should reveal how implicit attitudes contribute to methamphetamine use behavior when methamphetamine use disorder is initiated.

In summary, there is evidence that craving and methamphetamine dependence may be associated with automatic cognitive processes assessed with the IAT. To the best of our knowledge, the current paper is the first to show that the relationships between implicit attitudes and methamphetamine use problems can be significantly moderated by depression. These findings are consistent with dual model theory, which posits the influence of implicit methamphetamine-related cognitions on explicit amphetamine use behavior. Thus, exploring interventions targeting implicit attitudes in addition to explicit attitudes is warranted. Additionally, because the associations of implicit attitudes with outcomes for methamphetamine use appear to be more pronounced in depressive mood contexts, interventions might focus on helping individuals recognize the mood conditions under which they are most likely to relate to their issues of methamphetamine use. In particular, teaching individuals to exercise conscious control over methamphetamine use in depressive mood states may help to reduce the impacts that implicit attitudes have on methamphetamine craving and consumption.

Statement of Ethics

This study protocol was reviewed and approved by Institutional Review Board of Kaohsiung Medical University. Written informed consent was obtained if the patients agreed to participate in the study.

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Disclosure

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