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Relationship Between Gender and Psychotic Symptoms in Cocaine-Dependent and Methamphetamine-Dependent Participants

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Abstract

Background—It has been well documented that cocaine and methamphetamine use can lead to the onset of psychotic symptoms similar to schizophrenia. However, the research and literature on gender differences and stimulant-induced psychosis have been mixed.

Objective—The primary aim of this study was to investigate gender differences in the reporting of psychotic symptoms in cocaine-versus methamphetamine-dependent individuals.

Methods—Participants were recruited from the Los Angeles, California, community via radio and newspaper advertisements. All met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, criteria for cocaine or methamphetamine dependence, and all reported either methamphetamine or cocaine as their primary drug of abuse. During a screening interview, participants answered questions from the Psychotic Symptom Assessment Scale, which characterizes various types of psychotic symptoms during drug use (“while high”) or during periods of nonuse (“while abstinent”).

Results—Participants included 42 cocaine-dependent individuals (27 men, 15 women) and 43 methamphetamine-dependent individuals (25 men, 18 women). Among cocaine users, there were no significant differences between men and women with regard to ethnicity, years of use, route of administration, and amount used in the past week, though they differed significantly with regard to age ($P = 0.029$). In the “while abstinent” condition, women were significantly more likely than men to report experiencing auditory hallucinations (13% vs 0%, respectively; $P = 0.050$) and tactile hallucinations (20% vs 0%; $P = 0.016$), whereas men were more likely to report delusions of grandeur (48% vs 6%; $P = 0.006$). During the “while high” condition, women were significantly more likely than men to report delusions of grandeur (13% vs 0%, respectively; $P = 0.050$), tactile hallucinations (33% vs 0%; $P = 0.001$), and olfactory hallucinations (13% vs 0%; $P = 0.050$). Among methamphetamine users, there were no significant differences between men and women with regard to age, ethnicity, years of use, route of administration, or amount used in the past week. In the “while abstinent” condition, women were significantly more likely than men to

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report feeling that something was wrong with the way a part of their body looked (72% vs 32%, respectively; $P = 0.009$), olfactory hallucinations (39% vs 8%; $P = 0.010$) and dressing inappropriately (22% vs 0%; $P = 0.010$). During the “while high” condition, women were more likely than men to report delusions of grandeur (33% vs 16%, respectively; $P = 0.030$), paranoia (50% vs 16%; $P = 0.017$), and tactile hallucinations (61% vs 32%; $P = 0.050$).

Conclusions—The findings of the present study revealed that cocaine- and methamphetamine-dependent women were more likely than their male counterparts to report experiencing various psychotic symptoms. This information may be useful for clinicians and mental health professionals, who should take these symptoms into account as potential barriers that may impede effective treatment.

Keywords

cocaine; methamphetamine; stimulant; psychosis; gender

INTRODUCTION

Overall, it has been observed that males have exhibited significantly higher rates of substance use, abuse, and dependence.^{1,2} However, when investigating gender differences and the use of stimulants, it has been reported that females tend to have an increased likelihood of experiencing cocaine dependence.^{3,4} Similarly, it has been found that females may be particularly vulnerable to the reinforcing effects of stimulant drugs, such as cocaine or methamphetamine.^{5,6} In addition, females who seek treatment for substance abuse exhibit more social and psychiatric problems compared with males.⁷

It is well documented that the use of cocaine or methamphetamine is associated with increased prevalence of psychotic symptoms.^{8,9} The risk for the onset of these symptoms is quite high for male and female methamphetamine users. For example, 45% of methamphetamine users reported experiencing methamphetamine-induced paranoia, which was most likely experienced when those individuals used more than their typical amount of methamphetamine.¹⁰ In other reports investigating males and females, the prevalence of psychotic symptoms among methamphetamine users was 11 times higher compared with the general population, and nearly 25% of methamphetamine users experienced clinically significant levels of suspiciousness, unusual thought content, or hallucinations within the past year.¹¹ Similar findings have been reported in studies of male and female cocaine users. According to Brady et al,¹² at least 90% of cocaine users experienced paranoid delusions and 96% of cocaine users experienced hallucinations. In another study, Iwanami et al¹³ noted that cocaine-dependent patients were reported to experience a paranoid state similar to schizophrenia.

While stimulant-induced psychosis is common, the moderating effect of gender is less clear, and there are few reports investigating potential gender differences. One report found that males were more likely than females to experience cocaine-induced psychosis, including hallucinations or delusions.¹² Also, males who used their drug of choice via the intravenous route were more likely than females to experience amphetamine-related psychiatric disorders (including psychosis), while no differences existed between males and females who used via the nonintravenous routes.¹⁴

Research regarding the onset of psychotic symptoms in individuals who were not drug dependent has been inconclusive. For example, one particular study reported no gender differences for psychotic symptoms in schizophrenic populations,¹⁵ while others indicated that there was a higher incidence of psychotic symptoms reported in females.^{16–19} In the present study, we examined the prevalence of psychotic symptoms in cocaine-dependent

men versus women and in methamphetamine-dependent men versus women. The relationship between gender and stimulant-induced psychosis is an important topic to investigate, because it will provide insight into whether a particular gender is more susceptible to experiencing psychotic symptoms after cocaine or methamphetamine use/abuse. As a result, treatment providers can be made aware of the potential comorbidity between a patient's stimulant dependence and related psychosis so that treatment may be tailored to encompass both.

METHODS

Participants

Participants were recruited from the Los Angeles, California, community via radio and newspaper advertisements. All participants met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* criteria for cocaine or methamphetamine dependence, and none met criteria for concurrent methamphetamine and cocaine abuse or dependence. In addition, all subjects reported either methamphetamine or cocaine as their primary drug of abuse. The institutional review board of the University of California Los Angeles (UCLA) approved the study, and all subjects provided written informed consent. Participants were paid \$25 for completing the questionnaires.

Procedure/Measures

In a research facility at the UCLA Medical Center in Los Angeles, participants completed an initial battery of questionnaires including a demographic survey that focused on drug use history (eg, years, method of use, amount used per day, days of stimulant use in the past 30) as well as critical demographic information (eg, age, ethnicity). The quantity of cocaine or methamphetamine used was assessed by presenting the participants with test tubes containing various amounts (0.1–2.0 g) of white powder resembling cocaine or methamphetamine, from which they selected the test tube that best approximated their daily use. At the time of assessment, a toxicology screen was performed to assess recent substance use. The participants completed these assessments as part of the screening process for one of several medication development trials being conducted by our laboratory. The participants were screened by a research coordinator, one on one, in a private room where no one else could hear their responses.

Participants were also administered a variety of instruments designed to evaluate current mental health status, including the Structured Clinical Interview for *DSM-IV-TR* diagnoses (SCID)²⁰ or condensed version of the SCID (Mini-SCID),²¹ Beck Depression Inventory II,²² drug and alcohol use form (internal assessment), and Timeline Followback.²³ Participants met the following inclusion criteria: (1) regularly used either cocaine or methamphetamine (but not both); (2) were 18 to 55 years of age; and (3) were not seeking treatment for cocaine or methamphetamine use. In addition, participants did not meet any of the following exclusion criteria: (1) current Axis I psychiatric disorder (eg, schizophrenia, depression, bipolar, mania) or dependence on other drugs of abuse, other than their stimulant of choice or nicotine; (2) history of stroke, epilepsy, or brain injury; (3) history of violent criminal behavior or on parole; or (4) currently pregnant.

The key instrument used was the Psychotic Symptom Assessment Scale (PSAS),⁸ which consists of 32 questions that provide detailed information about psychotic symptoms. The test items, which are based on symptoms included in the *DSM-IV* criteria, assess the presence of delusions, hallucinations, disorganized thoughts (eg, ideas of reference, thought broadcasting, thought insertion), agitation, and ability to maintain focus. Analysis of the internal consistency of the test scales, which was indexed using Cronbach's α , showed that

each of the subscales yielded reliable data. Specifically, the following subscales were shown to be internally consistent: whether subjects had ever experienced particular psychotic symptoms ($\alpha = 0.87$), whether subjects had ever experienced psychotic symptoms during periods of nonuse (“while abstinent”) ($\alpha = 0.83$), and whether subjects had ever experienced psychotic symptoms during drug use (“while high”) ($\alpha = 0.86$).

Data Analysis

The *t* test was used to identify group differences across demographic and drug use profile data. The χ^2 analysis was used to determine whether cocaine- and methamphetamine-dependent participants differed with respect to the likelihood that they experienced a particular symptom while intoxicated versus while sober. The χ^2 analysis also was used to determine whether prevalence of psychotic symptoms differed across ethnic groups and route of administration. Simple linear regression was used to determine the level of association between drug use profile and cumulative onset of psychotic symptoms. *P* 0.050 was considered statistically significant. Statistical analyses were performed using SPSS version 11.0 (SPSS Inc., Chicago, Illinois).

RESULTS

Participants included 42 non-treatment-seeking, cocaine-dependent individuals (27 men, 15 women) and 43 non-treatment-seeking, methamphetamine-dependent individuals (25 men, 18 women) who were described previously.⁸ Table I provides demographic information for all participants. Cocaine-dependent men and women were similar with regard to ethnicity, years of use, route of administration, education, and the amount of money spent daily on the primary drug of abuse, although they differed significantly with regard to age ($P < 0.050$). Methamphetamine-dependent men and women did not significantly differ with regard to age, ethnicity, years of use, route of administration, education, or the amount of money spent daily on the primary drug of abuse.

In a comparison of cocaine-dependent men and women in the “while abstinent” condition, a significantly larger proportion of women reported hearing tapping noises, whispers, or music that others could not ($P = 0.050$) and feeling that someone was touching them when no one was there ($P = 0.016$). Cocaine-dependent men reported feeling like someone loved them from a distance even though that someone denied it ($P = 0.006$) (Table II). During the “while high” condition, a significantly larger proportion of cocaine-dependent women reported feeling like they had special powers ($P = 0.050$), feeling that someone was touching them when no one was there ($P = 0.001$), and smelling things that others could not ($P = 0.050$) (Table III).

In a comparison of methamphetamine-dependent men and women in the “while abstinent” condition, a significantly higher proportion of women reported feeling that something was wrong with the way a part of their body looked ($P = 0.009$), smelling things that others could not ($P = 0.010$), and dressing inappropriately ($P = 0.010$) (Table II). During the “while high” condition, a significantly higher percentage of methamphetamine-dependent women reported feeling like they had special powers ($P = 0.030$), felt their significant other was having an affair when it was not true ($P = 0.017$), and feeling strange sensations such as insects crawling on their skin ($P = 0.050$) (Table III).

DISCUSSION

As reported previously in a separate analysis examining the prevalence of psychotic symptoms in cocaine- and methamphetamine-dependent individuals, the overall frequency of psychotic symptoms was high.⁸ In the present study, we found that several psychotic

symptoms were more prevalent in women compared with men. Women reported paranoid and grandiose delusions, body dysmorphism, perceptual disturbances, and auditory, tactile, and olfactory hallucinations more frequently than did men. These findings are consistent with previous findings in both drug-using and non-drug-using individuals, and highlight important gender differences in the presence and persistence of psychotic symptoms.^{12,14–19}

One potential explanation for the increased prevalence of psychotic symptoms in women is that they used greater quantities of their drug of choice per day and for more years than did men. In the present study, the differences approached, but did not reach, statistical significance. The latter result does not negate the potential relationship between the elevated drug-use variables and the increased report of psychotic symptoms in women. For example, one investigation reported that cumulative duration of use predicted initial development of cocaine-induced psychosis.²⁴

The findings from this study indicate that women report more psychotic symptoms than men report, which is consistent with some of the general findings regarding gender differences and substance abuse. As it has been found that females are more likely to be affected by the reinforcing effects of stimulant drugs,^{5,6} it is reasonable to assume that females may be more likely to also experience psychotic symptoms that accompany cocaine or methamphetamine use.

Given the descriptive nature of this study, it is necessary to acknowledge that we did not evaluate a number of variables that could potentially moderate the association between gender and the onset of psychotic symptoms. For example, one study reported that crack-cocaine users who had a lower body mass index were more likely to develop cocaine-induced psychosis.²⁵ It may also be that estrogen and testosterone levels, and/or stimulant plasma levels, may affect the onset of psychosis. Males have achieved significantly higher plasma cocaine levels compared with females after administering intranasal cocaine in the laboratory.²⁶ In addition, it has been found that estrogen increases the reinforcing effects of stimulants for women.^{5,27,28} Furthermore, although the PSAS items are internally consistent, the external validity of the measure has not been evaluated (as we have not yet tested this questionnaire in another set of participants). Second, the present data reflect retrospective reports of psychotic symptoms by the participant rather than real-time assessment of psychotic symptoms by others. The data could be affected by recall bias,^{29,30} and reports of symptoms in hospitalized subjects would be valuable. For example, men may not feel as comfortable as women (or vice versa) providing accurate answers to some of the more “personal” questions. Also, participants suffering from intense psychosis and drug dependency may not be inclined to participate due to the severity of their illnesses. As a result, these data may not be representative of the entire cocaine-or methamphetamine-dependent population.

These findings may be important when investigating potential pharmacotherapies or behavioral therapies for cocaine and methamphetamine dependence. For example, pairing an antipsychotic medication with the primary pharmacotherapy or behavioral therapy being used may lessen the severity of psychotic symptoms. By doing so, clinicians may be able to reduce the intensity of psychotic symptoms that may “cloud” the judgment and focus of the affected individual. It is plausible that treatment success rates would increase, because cocaine- and methamphetamine-dependent individuals should be able to focus on treatment without the distraction of the hallucinations and delusions resulting from their previous cocaine and methamphetamine use. However, there are several adverse effects of these antipsychotic medications (eg, sedation, sexual dysfunction)³¹ that may interfere with or impede treatment success. In fact, it has been found that many individuals who are prescribed antipsychotics stop taking their medication due to adverse effects (approximately

two thirds of individuals participating in clinical trials stop taking their medication as well).³² As a result, these unpleasant adverse effects may mitigate the beneficial effects of antipsychotic medications.

Future studies will examine psychotic symptoms after administration of cocaine or methamphetamine in the laboratory. In addition, we will specifically assess gender differences and the effects that males versus females have in response to cocaine or methamphetamine administration. Although we did not notice gender differences after cocaine or methamphetamine administration in the laboratory (using the Brief Psychiatric Rating Scale), we intend to create a much more detailed scale for assessing various psychotic symptoms in the future.

Taken together, these data suggest that gender may play an important role in the experience of stimulant-induced psychotic symptoms, and we offer several factors that might contribute to these differences. Overall, women were more likely than men to report experiencing various psychotic symptoms in both the abstinent and high conditions. As a result, treatment providers should take this variability into account by tailoring substance abuse treatment plans to the individual and by factoring in potential comorbid symptoms.

CONCLUSIONS

The findings of the present study revealed that cocaine- and methamphetamine-dependent women were more likely than their male counterparts to report experiencing various psychotic symptoms. This information may be useful for clinicians and mental health professionals, who should take these symptoms into account as potential barriers that may impede effective treatment.

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Table 1

Demographic and substance use data for cocaine-dependent and methamphetamine-dependent participants. Data are mean (SD), unless otherwise indicated.^{8*}

Variable	Cocaine			Methamphetamine		
	Men (n = 27)	Women (n = 15)	P	Men (n = 25)	Women (n = 18)	P
Age, y	41.9 (6.7)	36.3 (9.2)	0.029	38.6 (9.0)	37.9 (8.9)	0.825
Race/ethnicity, no. (%)			0.953			0.886
White	3 (11.1)	3 (20.0)		13 (52.0)	10 (55.6)	
African American	17 (63.0)	8 (53.3)		6 (24.0)	2 (11.1)	
Hispanic	6 (22.2)	2 (13.3)		3 (12.0)	4 (22.2)	
Other	1 (3.7)	2 (13.3)		3 (12.0)	2 (11.1)	
Years of use	14.5 (8.7)	15.9 (10.0)	0.650	8.1 (7.1)	12.3 (10.0)	0.112
Route of administration, no. (%)			0.312			0.130
Nasal	8 (29.6)	3 (20.0)		2 (8.0)	4 (22.2)	
Smoking	18 (66.7)	12 (80.0)		12 (48.0)	12 (66.7)	
Intravenous	0	0		8 (32.0)	0	
Other	1 (3.7)	0		3 (12.0)	2 (11.1)	
Education, y	13.4 (2.4)	11.9 (2.4)	0.052	14.2 (2.4)	13.2 (2.2)	0.184
Days used in the past 30	15.9 (9.0)	16.7 (9.1)	0.780	16.2 (9.5)	17.3 (9.7)	0.713
Amount used per day, g	0.7 (0.5)	1.1 (1.0)	0.116	0.4 (0.4)	0.9 (1.2)	0.061
Amount spent per day, \$	48.9 (79.8)	55.5 (76.8)	0.797	21.0 (17.7)	28.6 (22.7)	0.245

*. Percentages may not equal 100 due to rounding.

Table II

Men and women differed significantly in reporting certain psychotic symptoms while abstinent from stimulants.*

Cocaine	Men, % (n = 27)	Women, % (n = 15)	χ^2	P
Have you ever felt that someone loves you from a distance, even though they deny it?	48	6	7.47	0.006
Have you ever heard tapping noises, whispers, or music that others couldn't hear?	0	13	3.78	0.050
Have you ever felt like someone is touching you but no one was there?	0	20	5.82	0.016
Methamphetamine	Men, % (n = 25)	Women, % (n = 18)	χ^2	P
Have you ever felt like something was wrong with the way a part of your body looked?	32	72	6.78	0.009
Have you ever smelled things that others could not?	8	39	6.03	0.010
Have you ever been aware of dressing inappropriately or unusually? Here, inappropriate or unusual means dressing as you would not usually.	0	22	6.13	0.010

* No other symptoms assessed reached statistical significance.

Table III

Men and women differed significantly in reporting certain psychotic symptoms while high on stimulants.*

Cocaine	Men, % (n = 27)	Women, % (n = 15)	χ^2	P
Have you ever felt like you have special powers?	0	13	3.78	0.050
Have you ever felt like someone is touching you but no one was there?	0	33	10.22	0.001
Have you ever smelled things that others could not?	0	13	3.78	0.050
Methamphetamine	Men, % (n = 25)	Women, % (n = 18)	χ^2	P
Have you ever felt like you have special powers?	16	33	4.44	0.030
Have you ever felt like your significant other was having an affair when it was not true?	16	50	5.74	0.017
Have you ever felt strange sensations, such as insects crawling on your body or skin?	32	61	3.60	0.050

* No other symptoms assessed reached statistical significance.