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Prevalence of Psychotic Symptoms in Substance Users: A Comparison across Substances

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Abstract

Background—Psychotic symptoms (delusions and hallucinations) are reported to be increased among persons using illicit substances but little is known about the comparative frequency with which the symptoms occur with abuse of different substances. To establish this, we interviewed individuals who had wide experience of commonly used drugs.

Methods—476 IV drug users, crack-cocaine users and heroin snorters recruited via street outreach were interviewed using the Composite International Diagnostic Interview – Substance Abuse Model (CIDI-SAM) to assess dependence on a number of substances including amphetamines, cannabis, cocaine, and opioids. As a part of this assessment, we assessed a history of delusions and hallucinations in the context of use of, or withdrawal from, these specific substances.

Results—From 27.8% to 79.6% of users of amphetamine, cannabis, cocaine, and opiates met DSM-III-R dependence for that specific substance. The prevalence of psychotic symptoms associated with each specific substance ranged from users with no diagnosis to users with severe dependence as follows: amphetamines (5.2% to 100%), cannabis (12.4% to 80.0%), cocaine (6.7% to 80.7%), and opiates (6.7% to 58.2%). The risk of psychotic symptoms increased for respondents who abused (OR=12.2) or had mild (OR=17.1), moderate (OR=47.0), or severe dependence (OR=114.0) on cocaine when compared to those who were users with no diagnosis. A similar pattern was evident in cannabis, opiate, and amphetamine users.

Conclusions—A majority of users dependent on illicit substances experience psychotic symptoms in the context of use of, or withdrawal from, these substances. Psychotic symptoms increased with the severity of the substance use disorders for all four substances. These findings emphasize the importance of developing services to target this population as they are at a heightened risk for developing psychotic symptoms.

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Keywords

substance use disorders; psychosis; epidemiology

1. Introduction

Individuals with psychosis have a higher prevalence of substance use than the general population. For example, research indicates that nearly 50% of individuals with schizophrenia have a lifetime prevalence of substance abuse [1,2]. Additionally, the Epidemiologic Catchment Area (ECA) study found that individuals with schizophrenia and schizophreniform disorder were at a greater risk for substance use disorders than non-psychotic individuals [3]. Individuals with bipolar disorder have also been found at an increased risk for substance use disorders [4-7].

Furthermore, studies have found a higher prevalence of schizophrenia and other psychotic disorders among users of illicit substances, such as cannabis [8,9]. Furthermore, the role of cannabis as a risk factor for the onset of psychosis or schizophrenia has also received much attention in the literature [10-12]. There are many reports that the abuse of cannabis [13-15], amphetamines [16] or cocaine [17] pre-date the onset of psychotic symptoms.

Substance use is also associated with subclinical levels of psychotic symptoms. Much of the literature on this has come from studies involving pharmacological challenges with stimulants [18,19] or cannabis [20]. Recently many studies have explored the incidence and prevalence of below threshold psychotic symptoms in the general population [21-24]. These studies have shown that substance use, particularly cannabis, is associated with the occurrence of psychotic symptoms. However, the relationship between clinical psychotic symptoms and use of specific substances other than cannabis has received minimal attention in the literature. If an individual uses multiple illicit substances and has psychotic symptoms, there is little information to suggest which substance(s) is likely to be implicated. Furthermore, the mechanism through which different substances contribute to psychotic symptoms is far from being clear [25,26]. Thus, research comparing commonly used illicit substances and their association with psychotic symptoms is needed.

To our knowledge, no study has reported the prevalence of psychotic symptoms in relation to the use of specific substances among an out of treatment sample of substance users. Thus, our study examines: (1) the rate of substance abuse and dependence in the sample; (2) the prevalence of psychotic symptoms among users of specific substances; (3) the risk of psychotic symptoms as a consequence of amphetamines, cannabis, cocaine, and opioids.

2. Method

2.1. Participants

The data for this report come from a NIDA-funded longitudinal study targeting intravenous drug users, crack-cocaine users and heroin snorters – the St. Louis Effort to Reduce the Spread of AIDS Study (ERSA Study). This study aimed to reduce the spread of HIV among St. Louis' most vulnerable drug-using population while improving drug abuse treatment [27]. The project field work began in 1990 in two target sampling areas which were known by the St. Louis City Police and Health Departments to be areas with high rates of prostitution, drug use and HIV. Potential respondents for this study were initially contacted on the street by outreach workers hired by the City of St. Louis Health Department. Of a total of 500 subjects recruited by the outreach workers, 476 agreed to be in the study. All respondents signed a Washington University IRB approved informed consent, which among other things notified them that all

data were protected by a NIDA Certificate of Confidentiality. The detailed methodology of ERSA program can be found elsewhere [27].

2.2. Measures

Respondents were interviewed with the Composite International Diagnostic Interview—Substance Abuse Module (CIDI-SAM). The CIDI-SAM is a structured interview module focused on DSM-III-R substance use disorders that expands on the WHO Composite International Diagnostic Interview (CIDI) [28]. All respondents who acknowledged using a substance more than five times in their lifetime were asked about the use of cannabis, amphetamines, sedatives, club drugs, cocaine, heroin and other opiates, PCP, hallucinogens, and inhalants. For this paper, we are focusing on the most prevalent drugs: amphetamines, cannabis, cocaine, and opioids. [29]. There were no early skip outs in the CIDI-SAM so the respondents were required to answer questions across the entire range of symptoms rather than just screening questions [30].

The CIDI-SAM included an extensive number of questions asking about symptom items that operationalized DSM-III-R criteria for substance abuse and dependence. DSM-III-R defined substance abuse as “a maladaptive pattern of psychoactive substance use” that was never severe enough to warrant a diagnosis of dependence. DSM-III-R described two abuse criteria (31, pp. 169) and required a simple threshold: at least one of two criteria must be endorsed in order to make a positive diagnosis. A substance abusing respondent may however meet both criteria, but not be dependent on the same substance; DSM-III-R defined nine possible criteria for dependence (31, pp.167-168), of which three or more must be present for at least a month or have occurred repeatedly over time to establish a positive substance dependence diagnosis. Thus, for each specific drug, the respondents were diagnosed as a) not having a substance use disorder diagnosis, b) having substance abuse only or c) dependence with or without abuse. DSM-III-R has also defined criteria for assessing the severity of substance dependence, which were operationalized in the CIDI-SAM as mild (3 or 4 criteria met), moderate (5 or 6 criteria met), and severe (7 to 9 criteria met) dependence.

Comparisons of the CIDI-SAM to clinician ratings have indicated that the CIDI-SAM is both reliable and valid in assessing substance use disorders [32,33]. The protocol for administration of the CIDI-SAM requires rigorous training, and for this study all interviewers underwent a one-week course of intensive study. Upon completion of the training each interviewer was required to complete a certification interview. Quality control was assured throughout the project by having all interviews reviewed by the project coordinator with weekly feedback given to the interviewers regarding any errors.

The presence of psychotic symptoms was operationalized using each drug category endorsed from two sets of questions in the CIDI-SAM. The *first set* asked: “While using (SPECIFIC DRUG) did it cause you any psychological problems like ‘Feeling paranoid or suspicious of people?’ While using (SPECIFIC DRUG) did it cause you to ‘See, hear, smell, or feel things that weren’t really there?’ If the respondent indicated yes, they were asked “Did either of these problems last for a month or more or occur several times?”

For the *second set* of questions, participants were presented with a list of withdrawal symptoms for each drug category endorsed, and among the symptoms was: “During the first few hours or days after using (SPECIFIC DRUG), did you ‘see, hear or feel things that weren’t there?’ Thus, the presence of psychotic symptoms were coded “0” or “not present” if the respondent answered negatively to both sets of questions and “1” or “present” if the respondent answered affirmatively to both items in question set 1 or to the single item in question set 2. These questions allowed us to analyze the presence of psychotic symptoms in the context of abuse of, or dependence on, specific substances.

Age was calculated from the birth month and year, and the interview month and year; the question was self-report. Gender was observed and coded “0” for male and “1” for female. Education was obtained by asking participants the extent of their educational attainment and then coded “1” for at least graduated high school and coded “0” otherwise. Marital status was obtained by asking participants to report their marital status and coded “1” for married and “0” otherwise, including single, divorced, or widowed. Employment status was obtained by asking participants if they were currently employed full-time, part-time, or if they were unemployed, and coded “1” for full-time and “0” for those who were unemployed or employed part-time.

2.3. Data Analysis

All analyses were conducted using SAS 9.1. The prevalence of substance abuse and dependence in the study sample and the prevalence of psychotic symptoms among substance users were estimated. Differences regarding the prevalence of psychotic symptoms by the severity of substance use were estimated with a chi-square analysis. The risk relationship between substance abuse and dependence severity and psychotic symptoms was examined with a logistic regression. We also examined age, gender, and employment status as covariates due to evidence that a younger age, male sex and the unemployed are at greater risk for substance use disorders [34,35].

3. Results

3.1. Descriptive statistics

The sample consisted of 424 individuals of whom 342 were male (71.9%) with a mean age of 32.2 years (SD=6.6, range 18 to 57 years). The participants were largely African-American (89.1%), with the majority high school graduates (53.3%). Nearly half were married (45.6%); over a quarter were employed full-time (25.4%).

3.2. Bivariate analyses

As shown in Table 1, over three-quarters of cocaine users met criteria for cocaine dependence. The comparative figures for opiate dependence were 63.1%, 50% for cannabis and 27.8% for amphetamines.

As shown in Table 2, the rates of psychotic symptoms were found to increase as the severity of use for each specific substance increased from no diagnosis to severe dependence. Only 6.7% of cocaine using respondents who did not meet criteria for a cocaine diagnosis of abuse or dependence had psychotic symptoms. This prevalence increased to 47.7% in respondents who abused cocaine, 55.2% in respondents with mild dependence on cocaine, 77.7% in respondents with moderate cocaine dependence, and 88.7% in respondents with severe cocaine dependence. A similar pattern regarding the prevalence of psychotic symptoms was found in users of cannabis, opiates, and amphetamines. For instance, 100 and 80 percent of amphetamine and cannabis severely dependent persons reported psychotic symptoms. Among all users of substances without a diagnosis of abuse or dependence, cannabis users reported the highest prevalence of psychotic symptoms (12.4%).

3.3. Multivariate analyses

As shown in Table 2, we found that participants who abused cocaine were over 12 times more likely than cocaine users without a cocaine use disorder (OR=12.2) to report having psychotic symptoms during use or withdrawal from cocaine (Table 3). Participants who had mild (OR=17.1), moderate (OR=47.0), or a severe (OR=114.0) dependence on cocaine were also at a greater risk than cocaine users without a cocaine use disorder to report having experienced psychotic symptoms during use or withdrawal from cocaine. Among the covariates, age was

found to be related to experiencing psychotic symptoms with older respondents being less likely to have psychotic symptoms (OR=0.96 CI=0.92,1.0, p=.047).

For the remaining substances, as use went from least to most severe, the risk of psychotic symptoms increased while controlling for age, gender, and employment status. The risk for psychosis was similar for abuse only and mild dependence among cannabis (OR=5.5 vs. OR=6.5) and opiate users (OR=4.8 vs. OR=6.0). However, there was a distinction regarding the risk for psychotic symptoms between abuse only and mild dependence among amphetamine users (OR=8.3 vs. OR=14.8). There was also a marked increase in the risk for psychotic symptoms when dependence became moderate or severe for cannabis (OR=25.1, OR=26.8; respectively) or opiate users (OR=10.1, OR=19.7, respectively). Moderate dependence on amphetamines (OR=35.3) was also associated with a much higher risk for psychotic symptoms than abusers or those with mild dependence. All respondents (n=10) with severe amphetamine dependence reported psychotic symptoms, thus an odds ratio of ∞ was estimated due to the small sample.

4. Discussion

The descriptive findings from this study suggest that the majority of cocaine (79.6%), cannabis (50.7%), and opiate (63.1%) users in our sample had some level of dependence to the substances, while a minority of amphetamine (27.9%) users had developed dependence. Nearly half of the respondents who abuse cocaine (47.7%) or cannabis (44.8%) reported experiencing psychotic symptoms during the use or withdrawal of those specific substances, while more than half of the respondents who were dependent on cocaine (80%), cannabis (63.5%), amphetamines (56.1%), and opiates (53.1%) reported psychotic symptoms. Furthermore, the rate of psychotic symptoms experienced by users who were dependent on these substances increased as the severity of dependence increased from mild to severe. For example, 55.8% of participants with mild cocaine dependence experienced psychotic symptoms, while this prevalence increased to 77.7% and 88.7% in participants with moderate or severe cocaine dependence. This finding supports a strong dose-response relationship, suggested by Thirthalli and Benegal [26], between the experience of psychotic symptoms and severity of substance use.

The general population prevalence of isolated psychotic symptoms has varied from 17.5% in the Netherlands [4] through 25% in New Zealand [36] to 28% in the US [37]. The higher proportions found among abusers and dependent users of the substances in this study are consistent with other reports that more substance users experience psychotic symptoms [21-24]. Cocaine has a strong dopamine uptake inhibition action [38] and cannabinoid receptors regulate the release of dopamine [39,40]; thus this may explain the higher proportion of subjects moderately or severely dependent on cocaine or cannabis who are experiencing psychotic symptoms. Amphetamines also act on the brain by stimulating dopamine release [41,42]. Thus, to the extent that the substances differ in their neurochemical actions on the brain, their differential effects may yield important clues in the causation of psychotic symptoms.

Although psychotic symptoms were found to be common among these substance users, the risk for development of psychotic symptoms was found to vary by substance and severity of the substance use. Given our limitation in statistical power and sample, the risk ratios must be interpreted with caution. After adjusting for age, gender, and employment, our findings suggest that when compared to cocaine users with no diagnosis, an increasing severity of cocaine use from abuse (OR=12.2) to mild dependence (OR=17.1) to moderate dependence (OR=47.0) to severe dependence (OR=114.0) is associated with a greater risk of drug-induced psychotic symptoms during use or withdrawal. A similar pattern, although quantitatively less acute, was

found for cannabis, opiates, and amphetamines. Thus, the risk of psychotic symptoms from use or withdrawal with respect to cocaine, cannabis, opiates, and amphetamines users displayed an increase with the progression of abuse to dependence severity for each specific substance. This supports a strong dose-response relationship between the experience of psychotic symptoms and severity of cocaine, cannabis, opiate, and amphetamine use after adjusting for covariates.

Psychotic symptoms in the general population have been associated with risk factors such as a younger age and unemployment [37,43]. Consistent with prior research, we found that a younger age was related to a greater risk of psychotic symptoms, but only among individuals using cocaine. This study also found that psychotic symptoms are highly prevalent during substance use and/or withdrawal, which is independent from a diagnosed psychotic illness (e.g., schizophrenia, bipolar disorder). However, it is not yet clear whether the presence of psychotic symptoms in individuals without a psychotic disorder contribute to the development of a psychotic illness later in life. Thus, research is needed to examine whether a history of psychotic symptoms due to substance use and/or withdrawal affects an individual's neurobiology, thus increasing the risk of developing a psychotic disorder such as schizophrenia or bipolar disorder.

Our findings also have implications for the pathophysiology of psychotic disorders. For instance, given the increase in risk for psychosis among substance dependent individuals and that recent studies have demonstrated a link between adolescent substance use and the onset of psychosis in young adulthood [12,45], research is needed to study the neurobiology of substance induced psychosis. Thus, such studies will inform primary prevention for substance abusers at risk for psychosis. Our findings also speak to the importance of developing services to target out-of-treatment substance users who abuse or are dependent upon amphetamines, cannabis, cocaine, or opiates as they are at a heightened risk for developing psychotic symptoms.

There are some important methodological limitations in this study. First, this study recruited substance abusers who represent a population of non-treatment seekers. It is possible that psychotic symptoms may have provided a barrier to their treatment access. Second, only drug-related psychotic symptoms were reported, thus we provide a limited perspective on how psychotogenic substances are experienced. Third, our measure of psychosis was limited to the items of the CIDI-SAM, and was not representative of all domains of psychosis outlined in the DSM-IV [44]. Fourth, 74% of the subjects were dependent on more than one substance and the reader might question whether subjects could correctly attribute their psychotic symptoms to a particular substance. However, prior work with this sample regarding withdrawal suggests that they can correctly attribute their psychotic symptoms to specific substances [30]. Lastly, in order to reveal the risk relationship for the severity of dependence to psychotic symptoms, a larger sample of participants with dependence on amphetamines is needed.

In conclusion, our findings suggest a strong dose-response relationship between the prevalence of psychotic symptoms and severity of cocaine, cannabis, opiate, and amphetamine use among out-of-treatment users of these substances. Services need to be designed to engage these individuals in the treatment process.

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Table 1

Prevalence of substance abuse and dependence in study sample (n=476)

	Cocaine (n=435)	Cannabis (n=419)	Opiates (n=233)	Amphetamines (n=205)
No diagnosis	10.3%	23.7%	32.2%	46.8%
Abuse only	10.1%	25.6%	4.7%	25.4%
Dependence with +/- abuse	79.6%	50.7%	63.1%	27.8%

Table 2
Prevalence of psychotic symptoms among users of specific substances

	% with Psychotic Symptoms	χ^2	p-value
Cocaine users with:			
No diagnosis (n=45)	6.7		
Abuse only (n=44)	47.7		
Dependence * (n=346)	80.0	135.1	p<.0001
Mild (n=58)	55.2		
Moderate (n=94)	77.7		
Severe (n=194)	88.7		
Cannabis users with:			
No diagnosis (n=97)	12.4		
Abuse (n=105)	44.8		
Dependence * (n=208)	63.5	89.2	p<.0001
Mild (n=107)	48.6		
Moderate (n=56)	78.6		
Severe (n=45)	80.0		
Opiates users with:			
No diagnosis (n=75)	6.7		
Abuse (n=11)	27.3		
Dependence * (n=147)	53.1	52.2	p<.0001
Mild (n=17)	29.4		
Moderate (n=20)	45.0		
Severe (n=110)	58.2		
Amphetamine users with:			
No diagnosis (n=96)	5.2		
Abuse (n=52)	30.8		
Dependence * (n=57)	56.1	62.9	p<.0001
Mild (n=41)	43.9		
Moderate (n=6)	66.7		
Severe (n=10)	100.0		

* dependence is with or without abuse

Table 3
Severity of substance use as a predictor of psychotic symptoms^a

	O.R.	C.I.	p-value
Cocaine			
Abuse only	12.2	(3.2,45.7)	p<.001
Mild dep.	17.1	(4.7,62.3)	p<.0001
Moderate dep.	47.0	(13.1,168.5)	p<.0001
Severe dep.	114.0	(32.2,403.7)	p<.0001
Cannabis			
Abuse only	5.5	(2.7,11.4)	p<.0001
Mild dep.	6.5	(3.2,13.4)	p<.0001
Moderate dep.	25.1	(10.4,60.8)	p<.0001
Severe dep.	26.8	(10.3,69.6)	p<.0001
Opiates			
Abuse only	4.8	(1.0,24.2)	p=.057
Mild dep.	6.0	(1.5,24.4)	p=.013
Moderate dep.	10.1	(2.8,36.4)	p<.001
Severe dep.	19.7	(7.2,54.0)	p<.0001
Amphetamines			
Abuse only	8.3	(2.8,24.6)	p<.0001
Mild dep.	14.8	(4.8,45.5)	p<.0001
Moderate dep.	35.3	(5.1,246.5)	p<.001
Severe dep. ^b	∞	(1, ∞)	p=1.00

^aData adjusted for age, gender, and employment status.

^bOnly 10 cases available, all had psychotic symptoms.