



The relative prevalence of schizophrenia among cannabis and cocaine users attending addiction services

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ABSTRACT

Background: Cannabis and cocaine are the most common illicit drugs for which people are treated in addiction services in Latin America. Much research has suggested that the use of cannabis increases the risk of schizophrenia; there is less evidence concerning cocaine. The aim of the present study was to establish the relative prevalence of schizophrenia in people treated for cannabis use and cocaine use disorders in Chile.

Methods: A sample of 22,615 people treated for illicit drug use disorders was obtained from a national registry of addiction service users in Chile. Clinical diagnoses were established at admission to substance use treatment programs or at any point during the period of treatment. Prevalence rates of schizophrenia and related disorders, and affective disorders were calculated for the groups of people with cocaine use disorders, and cannabis use disorders. Odds ratios (OR) for schizophrenia and for affective disorders were calculated for cannabis users using the group of people treated for cocaine use disorders as reference category.

Results: The prevalence of schizophrenia and related disorders was 1.1% in those with cocaine use disorders, but 5.2% in those with cannabis use disorders (OR 4.9; $p < 0.01$). The prevalence of affective disorders was 9.3% in cocaine use disorders, and 13.2% in cannabis use disorders (OR 1.5; $p < 0.01$).

Conclusions: The prevalence of schizophrenia and to a lesser extent affective disorders is higher among people with cannabis use disorder than cocaine use disorder among those attending addiction services.

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1. Introduction

Cannabis is the most commonly used illicit drug worldwide (Hall and Degenhardt, 2007; United Nations Office on Drugs and Crime, 2016). Its use has been consistently associated with an increased risk of psychosis (Radhakrishnan et al., 2014; Murray and Di Forti, 2016). Frequent users of cannabis have a two-fold increased risk of psychosis compared to non-users (Moore et al., 2007), and the risk appears to increase with the dose and frequency of use (Henquet et al., 2005; Moore et al., 2007; Zammit et al., 2002; Marconi et al., 2016), as well as in those who use more potent cannabis (Di Forti et al., 2009; Di Forti et al., 2014; Murray et al., 2016). One report suggests that people with a lifetime diagnosis of cannabis dependence have a 3.5 fold increased risk to have a

lifetime diagnosis of non-affective psychosis, and are twice as likely to have mood disorders (Agosti et al., 2002).

Cocaine is the second most commonly used illicit drug after cannabis in Latin America (Inter-American Drug Abuse Control Commission, 2015). Although other stimulants and especially amphetamines increase the risk for acute and temporary psychoses (Hermens et al., 2009; Niemi-Pynttari et al., 2013; Paparelli et al., 2011), evidence concerning a possible association between cocaine use and schizophrenia is still inconclusive.

Among those attending addiction services in Latin America, cocaine use is by far the most common problem followed by use of cannabis (United Nations Office on Drugs and Crime, 2016). Given the robust association of cannabis and schizophrenia in the general population and in clinical samples, whereas cocaine use mostly associates with acute temporary psychoses, we hypothesized that people using services for cannabis use problems had higher rates of schizophrenia than people using services for cocaine use disorders. The aim of the present study was to establish the relative prevalence of schizophrenia and affective disorders in people treated for cannabis and/or cocaine use disorders in public addiction services in Chile.

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2. Methods

2.1. Study population

A nationwide registry from the National Prevention and Rehabilitation Service for Drug and Alcohol Use in Chile (Servicio Nacional para la Prevención y Rehabilitación del Consumo de Drogas y Alcohol, SENDA) was studied. SENDA provides public health services for the assessment and treatment of people with substance use disorders, and covers about 80% of the population in Chile. The remaining 20% are treated in private addiction services. SENDA collects data on people at admission to outpatient and residential care treatment programs throughout the country.

The database comprised 30,502 people, who entered substance use treatments from January 2007 to October 2013. We studied those 22,615 people who had substance use disorders according to the International Classification of Diseases tenth edition (ICD-10) and their principal drug of addiction was cannabis and/or cocaine products (inhaled cocaine and smoked cocaine as base paste). We excluded patients who were primarily addicted to alcohol; however, people with primary addiction to cocaine and/or cannabis and comorbid alcohol use disorders were included.

2.2. Variables

Socio-demographic data were collected. The following variables were extracted from the database: 1) Gender, 2) Age at admission to treatment, 3) Primary drug of abuse indicated by the patients as causing the addiction problem and motivating their request for treatment, 4) Secondary drugs used (other substances of harmful use or dependency), 5) Age of initial use of primary drug, 6) Educational level, and 7) Comorbid mental disorder (if present). The following variables were calculated based on the available data: 9) number of years of use of the primary drug, 10) starting use of the primary drug before the age of 18.

2.3. Assessments

All addiction service users were clinically assessed for substance use disorders and comorbid mental disorders at their enrollment in the treatment programs. In addition, comorbid mental disorders may have been diagnosed at any point of time during the treatment. General physicians and psychiatrists in the treatment facilities assessed mental disorders using ICD-10 criteria in clinical interviews. When a psychotic disorder is present, diagnoses are usually confirmed by psychiatrists.

2.4. Study design

The study was cross-sectional, based on a nationwide database of public addiction service users. The sample was divided into three groups according to the drugs of use: 1) Users of cocaine based products without use of other illicit drugs; 2) Cannabis users without other illicit drug use; and 3) Users of both cannabis and cocaine.

Comorbid mental disorders were the outcome variables. The disorders studied were: 1) Schizophrenia and related psychoses (SCZRP) (ICD-10: F20–29); and 2) Affective Disorders including major depression and bipolar disorders (ICD-10 Code: F30–39) were studied as a comparison.

2.5. Statistical analysis

Descriptive statistics were used to describe socio-demographic variables for the three different groups of substance use disorders. The variables were gender, age at admission to substance use treatment, age at first use of the primary substance, first use before the age of 18 years, years of use of the primary drug, duration of treatment, comorbid alcohol use disorder, educational level and comorbid mental disorders.

Logistic regression analyses were conducted with the groups of drug use disorders as independent variables and the groups of psychiatric disorders as dependent variables. To compare the risk of psychiatric disorders in those with cocaine use disorder versus those with cannabis use disorders, the group with cocaine use disorders without other illicit drug use was the reference category. Odds ratios (OR) and 95% confidence intervals of the odds ratios were calculated. Multivariate analyses were conducted for each group of psychiatric disorders adjusting for gender, age at admission to substance use treatment, age at first use of the primary substance, comorbid alcohol use disorder and educational level.

To explore a possible effect of severity of cannabis use, we subdivided the group of users of both cannabis and cocaine into two subgroups: 1) using cannabis as primary drug and cocaine as secondary 2) using cocaine as primary and cannabis as secondary drug. We propose that people using cannabis as the primary drug had a more severe use of cannabis than those using it as secondary drug. In the subgroup that used cannabis as primary drug, cannabis was the primary problem causing people to use addiction services.

We calculated the ORs and 95% CI of the ORs for SCZRP for both subgroups compared to the reference category.

Statistical analyses were conducted using the software package R 3.01.

2.6. Ethical considerations

This work was carried out with the ethical authorization of SENDA. Data used in this study were part of the routine clinical data collection in public treatment facilities for substance use disorders. Researchers accessed processed and analyzed anonymized data. Identity and confidentiality of the patients were protected. Patient identifiers were encoded with an alphanumeric code untraceable to the individual.

3. Results

3.1. Socio-demographic characteristics and groups of drug use disorders

The sample comprised 74.1% of the total population entering public substance use services. Regarding the primary drug of use, 20.9% had harmful use, and 79.1% dependence. The majority were male (72.3%), and their ages ranged from 18 to 77 years, with a mean age of 31.7 (standard deviation 8.3); 75% were younger than 37 years. 35.8% of the sample were in basic outpatient treatment (one contact per week), while 42.6% received intensive outpatient treatment (two to five contacts per week) and 21.6% underwent residential treatment. The mean duration of treatment was 217 days with a standard deviation of 163 days, and the median duration was 172 days.

Cocaine was used by 94.4% of the sample, alcohol by 71.6%, and cannabis by 57.9%. Among the cocaine users, 79.5% inhaled cocaine, and 48.8% smoked it as base paste. 88.5% of the sample reported cocaine as their primary drug of use while 11.5% reported cannabis as their primary drug of use.

Table 1 shows characteristics of the patients grouped according to their use of cannabis and/or cocaine: 1) cocaine without other illicit drug use 2) cannabis without other illicit drug use and 3) use of both cocaine and cannabis.

A majority in all groups was male, had low educational levels and comorbid alcohol use. The mean age of enrollment in treatment was in the early thirties and did not differ between groups. The group of cannabis users without other illicit drug had an especially young age of onset with a majority initiating use before the age of 18 years and particularly long duration of the disorder.

Table 1
Groups of patients with cocaine and/or cannabis use disorders.

	Cocaine	Cannabis	Cocaine and cannabis
Total	9526 (42.1%)	1265 (5.6%)	11,824 (52.3%)
Male	6526 (68.5%)	937 (74.1%)	8879 (75.1%)
Age at admission (years)	33.4 ± 8.4	32.1 ± 10.5	30.2 ± 7.7
Age of first use (years)	23.1 ± 8.1	17.2 ± 5.3	20 ± 6.6
First use < 18 years of age	2582 (27.3%)	829 (66.2%)	4969 (42.2%)
Years of drug use	10.42 ± 7.4	15.02 ± 10.3	10.3 ± 7
Problematic alcohol use	6477 (68.0%)	1002 (79.2%)	8714 (73.7%)
<i>Educational level</i>			
Incomplete primary	1258 (13.3%)	147 (11.8%)	1240 (10.5%)
Primary	3520 (37.2%)	431 (34.5%)	4575 (38.9%)
Secondary	3880 (41%)	556 (44.4%)	5043 (42.9%)
Tertiary	806 (8.5%)	117 (9.4%)	896 (7.6%)
<i>Comorbid mental disorder</i>			
Schizophrenia and related psychoses	107 (1.1%)* 95% CI (0.9%–1.4%)	66 (5.2%)* 95% CI (4.1%–6.6%)	274 (2.3%)* 95% CI (2.1%–2.6%)
Affective disorders	882 (9.3%)* 95% CI (8.7%–9.9%)	167 (13.2%)* 95% CI (11.4%–15.2%)	1025 (8.7%)* 95% CI (8.2%–9.2%)

* $p < 0.001$.

3.2. Prevalence of comorbid mental disorders

Table 1 shows the prevalence of comorbid mental disorders for the different groups of drug use disorders. The prevalence of SCZRP was 1.1% in users of cocaine without other illicit drug use. The prevalence of SCZRP in users of cannabis without other illicit drug use was 5.2%. Users of both cannabis and cocaine had 2.3% prevalence of SCZRP. Rates of affective disorders were 13.2% in the group of cannabis users without other illicit drug (13.2%), 9.3% in the group of cocaine users without other illicit drugs, and 8.7% in the users of both cocaine and cannabis.

3.3. Odds for schizophrenia and related psychoses

Table 2 shows the raw and adjusted odds ratios with 95% confidence intervals for psychiatric disorders in the groups of users of cannabis without other illicit drugs in relation to cocaine users without use of cannabis or other illicit drugs (reference group). The odds ratios were adjusted for: gender, age at admission to substance use treatment, age at first use of primary drug, alcohol use, and educational level.

The chances of having SCZRP were highest in the group of users of cannabis without other illicit drug use, followed by the group of users of cannabis and cocaine, compared to the cocaine users who did not use any other illicit drugs.

In a subsequent analysis, we compared those who used cannabis as their primary drug and those who used it as a secondary drug, among the group of users of both cannabis and cocaine. Those who used cannabis as their primary drug had a greater risk to have SCZRP (crude OR 3.88; 95% CI: 2.79–5.39 and adjusted OR 3.99; 95% CI: 2.71–5.89), than the users of cannabis as secondary drug (crude OR 1.87; 95% CI: 1.48–2.36 and adjusted OR 1.78; 95% CI: 1.40–2.26).

Table 2
Crude and adjusted odds ratios for mental disorders in patients with cocaine and/or cannabis use disorders. Users of cocaine without other illicit drugs are the reference group.

	Cocaine (reference group)		Cannabis		Cocaine and cannabis	
	OR		Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Schizophrenia and related psychoses	1		4.85 (3.54–6.62)*	4.32 (3.03–6.18)*	2.08 (1.67–2.62)*	1.92 (1.52–2.42)*
Affective disorder	1		1.49 (1.25–1.78)*	1.58 (1.30–1.92)*	0.93 (0.85–1.02)	1.07 (0.96–1.12)

Adjusted for: gender, age at admission to substance use treatment, age at first use of principal substance, alcohol use, and educational level.

* $p < 0.001$.

3.4. Odds ratios for affective disorders

Table 2 presents the chances for affective disorders in the different groups of substance users. The group of cannabis users without other illicit drug use shows a higher prevalence of comorbid affective disorders than the reference group of cocaine users without other illicit drug use. Users of both cocaine and cannabis were not at significantly different risk from the reference group.

Among the covariates only gender showed statistically significant association with the outcomes, modifying the crude odds ratios as presented above in the adjusted models. Comorbid alcohol use disorders did not significantly mediate the above findings.

4. Discussion

4.1. Main findings

Our main finding is that while the prevalence of SCZRP (1.1%) was not increased in cocaine users attending addiction services compared with that generally reported for the general population, that in cannabis users was increased over that expected (5.2%). Furthermore the chances to have SCZRP were almost five times greater among cannabis users than cocaine users.

It is difficult to know how the rates of affective disorder that we found would compare with the general population as different studies report widely varying rates depending on the definition used. Nevertheless, again the chances to have an affective disorder were greater (OR = 1.5) in cannabis than cocaine users.

4.2. Strengths and limitations

This is the first study to establish the prevalence of major psychiatric disorders in those attending addiction services in a large nationwide registry in Latin America. To our knowledge, this is also the first study that compares the risk of schizophrenia between those with cannabis use disorders and cocaine use disorders among addiction service users.

There are of course some weaknesses in our study. The diagnoses of mental disorders were derived from clinical routine interviews, not from structured interview schedules. The data registry did not inform which patients were evaluated by psychiatrists and which by general practitioners. The quality of the routine diagnoses in the registry has not been investigated. A further limitation arises from the cross-sectional design of the study that did not allow causal inferences on the relationship between drug use and major mental disorders.

4.3. Comparison with the literature

The association between cannabis and stimulants with schizophrenia has been studied in clinical samples primarily treated for psychoses. Among patients with their first episode of psychosis, cannabis is the most commonly used illicit substance (Sara et al., 2013; Di Forti et al., 2014; Murray et al., 2016). Stimulants are also associated with drug-induced psychosis (Paparelli et al., 2011; Sara et al., 2013). In one study of people admitted to hospital for psychotic disorders and followed up for 2–5 years, cannabis use disorders predicted an increased likelihood of

progression to schizophrenia, while stimulant use disorders predicted a reduced likelihood (Sara et al., 2014a). In an eight-year follow-up of patients with substance-induced psychoses, people with cannabis use had higher risk of conversion to schizophrenia than people with amphetamine use (Niemi-Pynttari et al., 2013). Our findings support the view that cannabis use more strongly associates with schizophrenia in clinical practice than stimulant use.

In this present study, comorbid affective disorders were common in both types of illicit drug addiction, and as in the general population, more frequent than SCZRP. Cannabis use disorders were also significantly associated with affective disorders as compared to cocaine use disorders. However, the difference between the two types of illicit drug use disorders was less pronounced than for schizophrenia; and we did not find a stepwise increase in the group of people who used both drugs as for SCZRP.

There may be a dose effect, given that in subgroups of those who used cannabis and cocaine, the ones who used cannabis as primary drug had higher prevalence of schizophrenia than the ones who used cannabis as secondary drug. And both of the groups that used cannabis had higher risks of schizophrenia than the ones who only use cocaine products. Moreover, those who consult for cannabis addiction alone have higher risks of psychoses than those who use cannabis and cocaine products. Other research has pointed to a dose-response effect, reporting increased risk of schizophrenia particularly in those who use cannabis most frequently (Henquet et al., 2005; Moore et al., 2007; Zammit et al., 2002), and in those who use cannabis with higher delta-9-THC concentrations (Di Forti et al., 2009; Di Forti et al., 2014).

Lower age at first use of cannabis has been associated with increased risk of schizophrenia in the general population (Arseneault et al., 2002; Di Forti et al., 2014). In our study, the group that used cannabis without any other illicit drug had the earliest onset and longest duration of use. Adjusting in multivariate analyses, the age of first drug use did not explain the associations of cannabis use and schizophrenia.

The association between cannabis and schizophrenia has also been supported by neurobiological research (Luzi et al., 2008; Paparelli et al., 2011; Radhakrishnan et al., 2014). Cannabis can induce psychotic symptoms via delta-9-Tetrahydrocannabinol (THC), which acts on cannabinoid receptor type-1 (CB1). Cannabis may increase post-synaptic dopamine sensitivity. Cannabidiol (CBD) is another important component of cannabis, which has antagonistic effects on CB1 and which could attenuate psychotic symptoms induced by THC (Murray et al., 2016). In the last decades, the proportion of THC/CBD has increased in the plants for recreational use (ElSohly et al., 2016).

Cocaine use increases dopaminergic neurotransmission, which may relate to psychotic symptoms (Bradberry, 2002; Volkow et al., 2003). Population based epidemiological studies of cocaine use disorders and a possible relationship with schizophrenia are rare. Evidence is not yet conclusive. It has been reported that cannabis dependence is a major predictor of psychosis in cocaine-dependent patients (Roncero et al., 2013), which is concordant with our results.

The association between cannabis use and schizophrenia in addiction service users has clinical implications: addiction service providers should expect and assess schizophrenia symptoms especially in people consulting for cannabis use disorders. In the literature, there is much evidence that cannabis is a component cause of psychosis (Radhakrishnan, et al. 2014; Murray and Di Forti, 2016), although there remains some dissent (Hill, 2015; Ksir and Hart, 2016). Since our study is cross-sectional, we cannot determine the direction of effect. There is, however, agreement that the prognosis of people with psychosis who continue to use cannabis is poor (Barrowclough et al., 2014; González-blanch et al., 2015; Sara et al., 2014b; Schoeler et al., 2016). Such people require specialized treatment approaches for dual disorders addressing both the addiction and the psychotic symptoms (Horsfall et al., 2009).

4.4. Conclusions

Comorbid severe mental disorders are common in addiction service users. People who present for the treatment of cannabis use disorders are at an especially high risk to have comorbid schizophrenia. One in twenty people who consult with addiction services for cannabis use disorders may have SCZRP. In addition, affective disorders are somewhat more common in people treated for cannabis use than in people treated for the use of cocaine products. Service providers need to take this into account in running and planning addiction services.

Contributors

Nicolás Libuy performed the research question, design of the study and participated in editing the database and statistical analysis. Also participated in the write-up of each part of the manuscript. Robin Murray participated in design of the study, and wrote the manuscript. Carlos Ibáñez participated in obtaining the database in collaboration with SENDA and participated in the design of the study and wrote the manuscript. Valeria de Angel participated in editing the database, and reviewed the manuscript. Adrian Mundt participated in the research question, design of the study and statistical analysis; also, participated in wrote the manuscript. All authors have approved the final manuscript.

Conflict of interest

The authors declare that there are no conflicts of interest.

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