

# Differences between Psychotic Disorders with Concurrent Cannabis Use and Cannabis-Induced Psychoses

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## Abstract

**Background:** The fact that Cannabis use can lead to psychotic symptoms has been recognized years ago. Moreover, when the patient is using cannabis, the distinction between a primary psychotic disorder and a cannabis-induced psychosis seems to be critical for the prognosis. However, few studies focused on the differences between these two diagnostic groups. We hypothesize that cannabis-induced psychotic disorders have particular demographic, premorbid and clinical features. Our objective was to identify main factors associated to cannabis-induced disorders.

**Methods:** We conducted a retrospective study for a period of twelve years, from January 2002 to December 2013. The study sample was composed of patients hospitalized in the psychiatric department, who reported cannabis-use, and those whose blood and urinary toxicological screening have shown cannabis use. Demographic, family and clinical features were assessed. Psychotic disorders were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition criteria (DSM-IV), and the study population was divided into two groups, according to causality link of the cannabis on the psychotic disorders.

**Findings:** The sample was composed of 75 patients. Overall, 53 (70.66%) were diagnosed as having a primary psychosis, and 22 (29.33%) were diagnosed as having cannabis-induced psychosis. Significant differences were observed in two domains, concerning family and clinical features. The multivariate data analysis using logistic regression has shown four predictors as being greater in the cannabis-induced psychosis group.

The first factor was the age below 25 years old. Subjects in the induced psychosis group were younger, having a median age of 25.1 years compared with 32.1 years for subjects in the cannabis-induced psychosis.

The second factor was the marital status. Single or separated subjects were developing more cannabis-induced disorders (Odds Ratio (OR), 2.5; 95% Confidence Interval (CI), 0.69-8.96 the Pearson's correlation factor ( $p$  0.09).

The third factor was family history of psychiatric disorders ((OR), 2.6; 95% CI, 1.14-5.9).

The last key factor was an early age on the exposure to the substance, below age of 25 years old (0.02).

**Conclusion:** Differences between substance-induced and comorbid substance-use disorders permit identification of predictors of a substance-induced psychosis. Those factors could help clinicians to classify correctly an early-phase psychotic disorder that co-occurs with substance use in order to challenge treatment and manage severe and persistent mental disorders.

**Keywords:** Cannabis; Psychosis; Mental disorder; Cannabis induced psychosis

## Introduction

Relationship between cannabis use and psychosis is well documented and recognized. But, the distinction between a primary psychotic disorder that co-occurs with the use of cannabis and a cannabis-induced psychosis seems to be critical for studying illness course and prescribing appropriate treatment. It is established that cannabis use can cause acute psychosis [1] and that it can even fasten the evolutionary course of pre-existing psychotic disorders [2-4]. Although, whether cannabis use can cause schizophrenia or other chronic psychotic disorders remains a controversy [5]. Few authors studied the relation between cannabis use and schizophrenia-spectrum and mood disorders. Cannabis use is commonly known to increase the risk of psychosis and to result in a poor prognosis for subjects having an established vulnerability to psychotic disorders.

Recent studies have focused on the association between cannabinoids and psychosis. But what makes some subjects more vulnerable to cannabinoid-induced psychosis is still unclear [6]. Cannabis exposure is considered to be a contributing cause which interacts with other known, such as genetic factors, leading to schizophrenia. D'Souza et al. have found that cannabis use may increase by two- to three the risk for developing schizophrenia [7]. Among individuals with chronic psychosis the rate of substance abuse is higher than in the general population [8,9]. Moreover, even if the rate of psychotic disorders among cannabis-users is not known, clinicians suggest that substance-induced psychoses can lead to chronic illness and disabling [10-12]. In spite of the significance of the present issue, we found that there have been few studies evaluating the differences between primary and cannabinoid-related psychotic disorders.

We hypothesize that cannabis-induced psychotic disorders have particular demographic, premorbid and clinical features. Our objective is to identify main factors associated to cannabis-induced disorders.

## Methods

### Study population

We conducted a retrospective study including inpatients experiencing acute psychosis. Psychotic disorders were defined by the DSM-IV [14]. We collected data during a period of twelve years (from January 2002 to December 2013), concerning patients who were hospitalized for a first phase of psychotic disorder, from the medical records, interesting both the hospitalization duration and the later follow-up.

All patients were followed for more than two years in the psychiatry department, in the University Hospital Fattouma Bourguiba, Monastir, Tunisia. Subjects were identified during their hospitalization in the psychiatric department and recruited after being clinically stable. Study subjects, aged from 15 to 65 years, had at least a Brief Psychiatric Rating Scale (BPRS) score of 15, and had used cannabis during the last 30 days before admission. We included patients who have reported by themselves cannabis-use, and those whose results of blood and urine toxicological screens conducted routinely our psychiatry department, have shown cannabis use. A total of 75 subjects were selected for the study.

### Research diagnostic assessments

The DSM-IV criteria were used in order to differentiate primary disorders and cannabinoid-induced disorders [14].

### Statistical methods of analysis

We divided the cases into two groups:

"Group 1" or "primary psychosis" and "group 2" or "cannabis induced psychosis" on the basis of DSM-IV criteria. We compared the two groups regarding the socio-demographic and clinical data.

We used the Statistical Package for the Social Sciences (SPSS) version 20 to perform the analysis.

## Results

The sample was composed of 75 patients. Overall, 53 (70.66%) were diagnosed as having a primary psychosis, and 22 (29.33%) were diagnosed as having cannabis-induced psychosis.

About two thirds of the study sample (60.9%) initiated cannabis use before the appearance of psychotic symptoms.

Among group 1 the diagnoses were: schizophrenia (n=19 (43.2%)), psychotic mood disorder (n=18 (40.9%)), brief psychotic or schizophreniform disorders (n=3 (6.8%)), and psychotic disorder not otherwise specified (n=4 (9.1%)).

Among group 2 the diagnoses were brief psychotic disorders/schizophreniform disorders (n=16 (51.6%)), mood disorders (n=9 (29%)), and schizophrenia (n=6 (19.4%)).

Age groups below 25 years old seem to be more concerned by cannabis use, with a rate of 32%. Duration of substance use was between three months and eighteen years, with a mean duration of five years. Two thirds of patients reported regular substance use. Route of administration was exclusively a respiratory route, in the form of hand-rolled cigarettes. 90% of individuals were tobacco smokers, and 37.5% were consuming alcohol drinks regularly.

For 37.5% of subjects, use of alcoholic drinks preceded cannabis use. Substances used were as follows: 54.7% for only cannabis use, 16% for cannabis and psychotropic drug use, 4% for cannabis and volatile solvents, and 6.6% for cannabis and other substances use (cocaine, heroin, ecstasy, Solanaceous plants).

### Comparison of socio-demographic characteristics

Table1 shows demographic and family characteristics for the whole sample and for the two groups.

Most subjects in both groups were male.

When we compared the primary and cannabis-induced psychosis, we noted two main differences:

Patients in group 2 were younger than those in group 1 (25.1 years vs. 32.1 years).

20.5% of group 1 were married compared to 6.5% in group 2. We found no significant difference on sex, level of education, and employment between the two groups.

### Comparison of clinical characteristics

Table 2 illustrates data about clinical characteristics for overall sample, primary disorder and substance induced psychosis groups. Developing a cannabis-induced psychosis is multiplied by 5 if the onset of the substance use preceded the onset of the psychiatric disorder. Mean hospitalization's duration was 17 days in both groups. We found no difference in duration of cannabis use between primary and cannabis-induced psychotic disorder.

We found no difference between the two diagnostic groups on the presence of delusions (60.37% versus 59.09).

**Table 1:** Demographic and family domain variables for overall sample, primary disorder and substance induced groups.

Variables	Subject Groups			OR	95% CI	p-Value
	Overall (n=75)	Primary Disorder (n=53)	Cannabis-Induced Psychosis (n=22)			
Sex (%)						
Male	96	95.4	96.8	1.2	[ 0.24;6.34]	0.8
Female	4	4.6	3.2			
Age (y)						
Median	29.23 ± 8.95	32.1 ± 9.7	25.1 ± 5.7	-	-	0.01
Marital Status						
Single/Separated	81.3	79.5	93.5	2.5	[0.69;8.96]	0.09
Married	13.3	20.5	6.5			
Level of education						
Primary/College	88	93.1	90.3	2.5	[0.96;6.57]	0.6
High school diploma	12	6.9	9.3			
Employment (%)						
Unemployed	65.3	68.2	64.5	1.1	[ 0.63;1.92]	0.7
Employed	34.7	31.8	35.5			
Parental mental illness (%)						
Yes	49.3	61.4	32.2	0.3	[ 0.11; .97]	0.01
No	50.7	38.6	67.8			

**Table 2:** Data about substance use and clinical characteristics for overall sample, primary disorder and substance induced groups.

Variables	Subject Groups				OR	95% CI	p-Value
	Overall (n=75)	Primary (n=53)	Disorder	Cannabis-Induced Psychosis (n=22)			
Age for Substance Use (y)							
Age at the beginning of the tobacco use, mean	18.8	19.2		18.3	-	-	0.6
Age at the beginning of the alcoholic drinks use, mean	19.7	19.8		19.5	-	-	0.9
Age at the beginning of the cannabis use, mean	23.1	27.9		20.15	-	-	0.2
Cannabis Use Duration (y)	5	4.8		4.6	-	-	0.9
Diagnosis Classification							
Schizophrenia	33.3	35.8		27.3	-	-	0.01
Mood disorders	36	50.9		0	-	-	
Brief psychotic or schizophreniform disorder	25.3	5.7		68.2	-	-	-
Psychotic disorder not otherwise specified	5.3	7.5		0	-	-	-
Delusions/ Hallucinations (%)							
Yes	50	60.37		59.09	-	-	0.4

No	50	39.63	40.91	-	-	-
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## Discussion

Cannabis, or marijuana, is the most commonly used illegal substance all over the world [15-17].

In 2013, the Word Drug Report There indicated that that was a minor increase in the prevalence of cannabis users (180.6 million or 3.9 per cent of the population aged 15-64) as compared with previous estimates in 2009 [18].

Most available studies [17,19-21] are providing great evidence that cannabis consumption can lead to acute, transient effects; acute, persistent effects; and delayed, persistent effects, of psychotic and affective experiences. Use of cannabis may be considered as a cause or a co-morbidity of mental disorder according to a temporal relationship; as the delay of consumption and the onset of psychosis [17].

### Limitations of the study

The current study focuses on the differences between psychotic disorders with concurrent cannabis use and cannabis-induced psychosis, and gives crucial data, yet we have met three main limitations.

The first limit was the retrospective analysis of data. Based on the information provided by medical records, it was complex to establish the chronology of disorders.

The second limit was the application of the DSM-IV criteria in order to differentiate the two groups and the lack of consideration of the updates made by the DSM5. In fact, our study was held from 2002 to 2013. Since, the approach of substance use disorders in DSM-IV has been closely revised. The knowledge about substance use disorders has been advanced notably. In order to take into account the advances, the DSM-V was published in 2013 [22,23].

### Description of the study population

The study had shown that 32% of subjects were aged between 17 and 25 years old, with a median age of 29 years. Cannabis is believed to have been introduced to Tunisia during the Arab invasions of the 9th through 12th centuries. Many countries in Africa reported seizures of cannabis, and particularly in Tunisia. Seizures of cannabis during the last years have increased, and continue to be concentrated in the North Africa [18].

Mabrouk et al. have shown in a recent study published in 2011, that mean age for Tunisian cannabis users was 25 years [24].; Lifetime use of cannabis was 1.4% according to the MedSPAD survey [25]. In other countries, nowadays, approximately 20% of young people report use at least once per week or heavy use (that means use more than 100 occasions) [26-28].

In the united states of America, in 2014 an estimated 6.8 million young adults aged 18 to 25 were using regularly

cannabis, that corresponds to 19.6 % of adults who use cannabis. In the same report, 6.6 % of adults aged 26 or older were current users of cannabis [29]. In fact, the youth constitutes a period of experiment, often including the experience of the drug, especially as the young people represent a particularly vulnerable and influenceable population.

Like almost all the previous studies, our study have shown that almost all of the subjects were male [8,30-32].

We have also noted that 81.3% were single or separated, having a primary or a secondary level of education in 88% of cases. This result is consistent with the study of Mabrouk et al. that interested a population coming from the same region as our study. In fact, they have found that 84.8% of individuals were single or separated, and that 93.6% of subjects have primary or secondary educational level [24].

### Comparison of socio-demographic characteristics

Three main static factors were identified regarding demographic and family characteristics, as associated with developing cannabis induces psychosis. Those factors should be early identified.

The first factor was the age below 25 years old. Subjects in the induced psychosis group were younger, having a median age of 25.1 years compared with 32.1 years for subjects in the cannabis-induced psychosis. This finding was consistent with the result found by Nunez and Gurpegui [34].

Even though most adolescents are using cannabis without harmful consequences, a minority experience negative outcomes and findings suggest that the most vulnerable to develop psychiatric outcomes are most likely the youngest cannabis users [1,35]. In contrast, Caton et al. [36] noticed that subjects with substance-induced psychosis were older.

The second factor associated with cannabis induced psychosis was the marital status. Single or separated subjects were developing more cannabis-induced disorders. This data strengthens those provided by Liraud et al. [37]. But Fergusson et al. [20] have reported that marital status should be considered as a confounding variable.

The third factor was family antecedent of psychiatric disorders. Patients with parental mental disorder are more likely to develop primary psychosis. Our findings were consistent with those found by other authors [7,38-40], and emphasizes the hypothesis of vulnerability to psychosis.

We have noticed no differences between the two groups regarding sex, educational level and employment status. A similar study published in 2005 emphasizes those findings [36].

An earlier age for exposure to cannabis was associated to an increasing risk for developing primary psychosis [1,36,40]. Arseneault et al. [1] have also noticed that an early cannabis use confers greater risk for schizophrenia outcomes later.

Miller et al. [38] confirmed that Cannabis use, use of other illicit substances and upsetting life events may all lead to psychotic symptoms in vulnerable young people.

### Comparison of clinical characteristics

Our results have not revealed differences between the two groups about the presence, type or severity of delusions or hallucinations.

Caton et al. [36] noticed that subjects with primary psychosis had notably more positive symptoms and that hallucinations in the substance-induced psychosis group were mostly visuals and that positive symptom were more severe.

### Conclusion

In our study subjects in the induced psychosis group were younger, single or separated with a family history of psychiatric disorders and an early age on the exposure to the substance compared to those with a comorbide use. Differences between substance-induced and comorbide substance-use disorders permit identification of predictors of a substance-induced psychosis. Those factors could help clinicians to classify correctly an early-phase psychotic disorder that co-occurs with substance use in order to challenge treatment and manage severe and persistent mental disorders.

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