REVIEW ARTICLE

Psychiatric Morbidity of Cannabis Abuse

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ABSTRACT

The paper evaluates the hypothesis that cannabis abuse is associated with a broad range of psychiatric disorders in India, an area with relatively high prevalence of cannabis use. Retrospective case-note review of all cases with cannabis related diagnosis over a 11-year period, for subjects presenting to a tertiary psychiatric hospital in southern India was carried out. Information pertaining to socio-demographic, personal, social, substance-use related, psychiatric and treatment histories, was gathered. Standardized diagnoses were made according to Diagnostic Criteria for Research of the World Health Organization, on the basis of information available.

Cannabis abuse is associated with widespread psychiatric morbidity that spans the major categories of mental disorders under the ICD-10 system, although proportion of patients with psychotic disorders far outweighed those with non-psychotic disorders. Whilst paranoid psychoses were more prevalent, a significant number of patients with affective psychoses, particularly mania, was also noted.

Besides being known as either the causative agent or a potent risk factor in cases of paranoid psychoses, cannabis appears to have similar capabilities with regard to affective psychoses, particularly in cases of mania. It is suggested that cannabis has the potential to act as a "life event stressor" amongst subjects vulnerable to develop affective psychoses and the possible aetiopathogenesis of such a finding is discussed.

Key words: Cannabis, psychiatric disorders

INTRODUCTION

Cannabis is one of the most frequently abused psychoactive drugs (Grinspoon and Bakalar 1993). Psychiatric disturbances associated with cannabis use range from minor psychological responses such as anxiety and panic (Thomas 1996), to depressive disorders (Troisi et al 1998), the more serious mental illnesses such as the putative 'cannabis psychosis' (Talbott and Teague 1969), acute functional psychosis (Johns 2001), chronic psychosis (Ghodse 1986) and the poorly validated entity of 'amotivational syndrome (Hall et al 1999). The nature of association and the direction of causality between cannabis use and various mental disorders await elucidation (Thomas 1993). The strongest evidence of

a specific contributory role of cannabis use exists only in relation to schizophrenia (Andreasen et al 1987).

India has a long tradition of cannabis use, which is often socially sanctioned (National Institute of Social Defense 1992). The association between cannabis use and mental disorders has been recorded for well over a century (Indian Hemp Commission Report 1894). Whilst considerable attention has been paid to the association between cannabis use and psychotic disorders (Basu et al 1999, Thacore and Shukla 1976, Chopra and Smith 1974), relatively little is known about the impact of cannabis abuse on wider psychiatric morbidity. We present a retrospective study as preliminary exploration to evaluate the hypothesis that cannabis abuse will be associated with a

broad range of psychiatric disorders, through a case-note review of patients abusing cannabis who presented to a large tertiary psychiatric hospital in south India. We also explored the pattern of cannabis use by this population.

METHODS

The Catchment Population: The study was conducted at a tertiary referral center in Bangalore, catering to a large catchment area. All patients receive a diagnostic code according to the criteria laid down in successive revisions of the International Classification of Diseases - ICD-9, (prior to 1992) and ICD-10 (thereafter). In keeping with WHO recommendations, all comorbid psychiatric diagnoses are coded for each patient.

Sample: Selected case-notes with any cannabis related diagnosis were identified for the period between 1984-1994.

Data: Information was recorded for socio-demographic data, history of substance use and other clinical history variables. Socio-demographic variables included subject's age, sex, completed years of education, and occupation. Substance use variables were age of onset of cannabis use, reason for initiation, duration of cannabis use, duration of daily use, temporal sequence of onset of psychiatric disorder in relation to cannabis use, and use of any other psychoactive substance prior to and following the onset of cannabis use. Further, family history of substance use and mental illness, and the reason for establishing contact with the hospital were recorded. Psychopathology variables recorded included delusions (reference, persecution, grandiosity, infidelity and others), hallucinations in any modality, thought disorder (including flight of ideas), thought alienation phenomena, psychomotor activity, mood disturbance, level of sensorium, cognitive deficits and treatment offered.

Information pertaining to psychopathology was recorded in the following manner:

a) for patients with 1-2 contacts during the study period, all phenomena displayed

during each of these contacts was recorded. In doing so, the 'present state' format for recording psychopathology was adopted.

b) for patients with 3-5 contacts, symptoms contained in the most recent contact were recorded along with symptoms of a similar type but with a more characteristic symptom profile, employing the notion of a 'representative episode'. Where the most recent episode of symptoms was different from the representative episode (for example, manic episode manifested upon a depressive representative episode) both sets of symptoms were recorded.

c) In cases with more than 5 contacts, all varieties of symptoms e.g. psychotic, affective and neurotic, as had been displayed by the patient, were recorded. Where there were two periods or episodes with different types of symptoms, these were rated as though they were sub-episodes of one extended episode employing the notion of symptoms experienced in the 'lifetime before'. This pattern is an acceptable method of symptom recording in order to generate diagnoses [World Health Organization 1993a]. All diagnoses were made on the basis of criteria laid down in the Diagnostic Criteria for Research, DCR, (World Health Organization 1993 b).

RESULTS

Socio-demographic data

Two hundred and forty four notes were identified as having a cannabis related diagnosis. All 244 subjects were male. Their mean age was 30 years (S.D. ± 9.7; Range = 18-82 years) and 53% were single (109/204; data unrecorded = 40). They had on average 9.7 years (S.D. ± 9.8) of education and 45% had received between 5-10 years of formal education. Sixty-two percent of patients were employed with representation of professional, skilled and unskilled workers being 13%, 27% and 22% respectively.

Substance use history

The mean age of initiation of cannabis use was 22.4 years (S.D. ± 8.4 years; Range = 10-65 years). Forty-three percent (9=105) had started using cannabis during the second decades of their lives. Eighty-nine (36%) began use during the third decade whilst twenty-five (10%) did so in the fourth decade. For the rest, onset of use was even later. Where information pertaining to reasons for cannabis use was recorded (n = 115; 47%), 57% cited recreational and experimental use, 12% attributed onset to a dysphoric mood state while 11% cited peer pressure as the primary reason.

Data was unavailable for total duration of non-continuous (regular but not daily) and continuous (daily) cannabis use in 32 (13%) and 141 (58%) cases respectively. The mean duration of non-continuous use of cannabis was 80 months (S.D. ± 71 months) while the duration of continuous use was 49 months (S.D. ± 50 months). Amongst daily users, 32 (31%) subjects had been using cannabis for less than 2 years, 44 (43 %) patients had been using it between 2-5 years and 27 (26 %) patients

had consumed it for over 5 years.

Relation of cannabis use to onset of psychiatric disorders

In 127 patients (52%), a psychiatric disorder had occurred following cannabis use while for 18 patients (7%), psychiatric disturbance had preceded the onset of cannabis use. Data were unavailable for 99 patients (41%). For 67% of patients cannabis was the first drug of abuse in their substance use life-trajectories. Alcohol and opioids were the initial substance of abuse in 29% and 4% patients respectively. Amongst those using cannabis on a continuous basis, 15% also used polysubstance (cannabis, alcohol and opioids for this study) while 11% and 9% used only alcohol and opioids respectively. Thus, 35% of cannabis users also used other substances concurrently, whilst for the remaining 65% cannabis remained the only substance of use. Data on homotypic comorbidity (other comorbid substance use disorders) was unavailable for 24 cases (see table 2).

TABLE 1 : Socio-demographic and substance use variables

Variable (N=244)	Mean	S.D.	Range
Age of patient	30 years	+_9.7 years	18-82 years
Age of onset of cannabis use	22.4 years	+_ 8.4 years	10-65 years
Duration of non-continuous cannabis use	80 months	+_ 71 months	1-244 months
Duration of continuous cannabis use	49 months	+_ 50 months	1-240 months

TABLE 2 : Temporal relation between cannabis and other drug use

(n =244)

	Substance used Following Cannabis		Preceding cannabis use	
	n	%	n	%
	64	29	1	11
Opiates	8	4	0	9
Combination of the above	2	1	34	16
None	146	66	139	63
Not known	24		24	

Family history

Data on family history were available in 202 (83%) subjects. 33 subjects (16%) had a positive family history of a psychiatric disorder and 48 (24%) had a positive family history of substance abuse. Twenty-seven percent of patients with non-psychotic illnesses had a positive family history followed by subjects with affective psychoses (26%), paranoid psychoses including schizophrenia (18%), cannabis psychosis (16%) and substance misuse disorders (9%). Patients with only substance misuse disorders had the highest rate of family history of substance misuse (32%), followed by subjects with non-psychotic illness (29%), paranoid

Psychopathology

Delusional thinking was reported in 105 patients (43%). Persecutory delusions were the commonest (26%) followed by grandiose (22%) and referential (9%) delusions. Forty-one percent of patients experienced hallucinations, most commonly in the auditory modality (25%). Thought disorder, including 'flight of ideas', was recorded in 26 patients (11%). Elated mood (23%) was more common than depressed mood (16%), in patients with affective disturbances. Thought alienation phenomena such as thought broadcasting, thought insertion and thought withdrawal were reported in 11

Diagnosis

Two types of comorbidity were identified in this cohort. Cannabis use disorder/s was either associated with other substance use disorder/s (but not with substance use related mental disorder/s) or with independent psychiatric disorder/s, i.e. non-substance use related. The former was referred to as homotypic while the latter as heterotypic comorbidity [Degenhardt et al 2001].

a) Substance abuse comorbidity (Homotypic comorbidity):

There were in all eight different types of substance related diagnoses, other than cannabis-related diagnoses, in the total cohort (see table 4). There were 144 cases of cannabis dependence, 95 cases of harmful use (abuse) and five cases of acute intoxication. One hundred nine patients (47%) also received another substance misuse disorder diagnosis, which included forty-nine cases of alcohol abuse (n=23) or dependence (n=26), thirty-six cases of polysubstance abuse (n=13) or dependence (n=23) and thirteen cases of opioid dependence. Polysubstance abuse/dependence was recorded in those abusing three different substances concurrently: cannabis, alcohol and opioids. There were no case of amphetamine, benzodiazepine, cocaine, ecstasy, LSD, inhalant or steroid abuse. The prevalence of nicotine and caffeine use was not recorded. Substance misuse/dependence was the only psychiatric diagnosis in eighty cases (34%). This number may appear to be smaller than what the preceding figures suggest as patient with more than one substance abuse/dependence were counted more than once under the respective headings. For instance a patient with cannabis abuse/dependence who was

TABLE 3 : Family history of mental illness and substance misuse

Diagnostic groups	Family History of Mental Illness (data unavailable n=42, 17%)		Family History of Substance Misuse (data unavailable n=41, 17%)	
	n	%	n	%
Non-psychotic	4/15	27	4/14	29
Affective psychosis (DCR rubric of F30-39)	8/31	26	4/30	13
Non-affective psychosis (DCR rubric of F20-29)	7/39	18	9/41	22
Cannabis psychosis	8/51	16	9/50	18
Substance misuse disorder	6/65	9	22/68	32
Total	33/202	16	48/203	24

psychoses (22%), cannabis psychosis (18%) and affective psychosis (13%).

Reason for help seeking

For 110 patients (56%) (Data unavailable: n= 47; 19%), display of abnormal behavior usually noted by family members formed the reason for establishing contact with the clinical services. A third of the patients contacted the hospital for relief from distressing withdrawal symptoms of alcohol and opioid withdrawal. Subjectively reported depressed mood was the presenting complaint in 11% patients.

(4%) cases. Increased psychomotor activity (n=11;4%), pressure of speech (n =9; 3%) and a combination of the two (n=7; 2%) were also evident in a small proportion of patients.. Bizarre behaviour that included such acts as smearing faeces, spitting, inappropriate and vacuous laughter, living in rubbish pits, taking off one's clothes, self mutilation, mutism, and posturing was reported in 31 (13%) cases. Catatonic symptoms were included amongst these. The case notes also recorded ten patients as having clouding of consciousness (4%), and seven patients (3%) with cognitive deficits
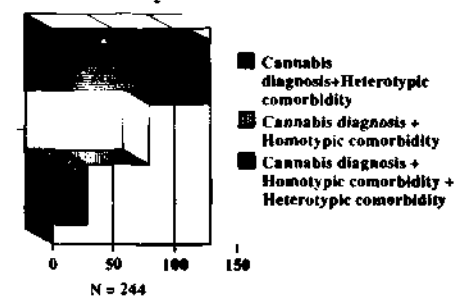
Comorbidity of Cannabis abuse

Cannabis diagnosis+Heterotypic comorbidity
Cannabis diagnosis + Homotypic comorbidity
Cannabis diagnosis + Homotypic comorbidity + Heterotypic comorbidity

N = 244

TABLE 4 : Psychiatric morbidity in patients abusing cannabis

Diagnosis	No. of cases	% (N=244)
Cannabis induced psychosis	51	21
Schizophrenia	35	14
Delusional disorder	5	2
Other non organic psychotic disorders	18	7
B.A.D-mania with psychosis	30	12
B.A.D.- severe psychotic depression	1	0.4
Severe psychotic depression	4	2
Hypomania	4	2
Mild depression	1	0.4
Moderate depression	3	1
Other depressive disorder	1	0.4
Cyclothymia	1	0.4
Dysthymia	2	1
Generalized anxiety disorder	1	0.4
Adjustment reaction - prolonged depression	1	0.4
Trance and possession disorder	1	0.4
Dissocial Personality disorder	1	0.4
Pathological gambling	1	0.4
Exhibitionism	1	0.4
Mild Mental Retardation	1	0.4
Cannabis induced unspecified mental & behavior disorder	1	0.4
Substance use/dependence only	80	34
Total	**244**	**100**

also abusing alcohol and opioids was coded under cannabis abuse and polysubstance abuse respectively.

b) Independent psychiatric disorder comorbidity (Heterotypic comorbidity)

Twenty-one heterotypic comorbid psychiatric diagnoses were made for 164 patients (67%), i.e. having a comorbid psychiatric disorder. Psychotic disorders were experienced by 144 patients (88% of

Heterotypic comorbidity

Heterotypic comorbidity of Cannabis use

those with comorbid psychiatric disorders), while 20 patients experienced a non-psychotic illness (12%). The group of patients with psychotic disorders was made up of those suffering with paranoid psychosis including schizophrenia (n=58; 40%), cannabis psychosis (n=51; 35%) and affective psychosis (n=35; 25%). Depressive and anxiety disorders (n=9; 45%) were the largest contributors to the numbers of those with non-psychotic disorders.

Cannabis psychosis was the commonest diagnosis amongst those with psychotic disorders. Six different subtypes of cannabis psychosis were diagnosed, the commonest subtype being a mania-like psychosis (n=22) with grandiose delusions, elated mood and increased psychomotor activity. A predominantly schizophrenia-like psychotic state (n=8) and a predominantly delusional state (n=6) were seen more often than a further six cases of a predominantly hallucinatory psychosis. Five subjects presented with a polymorphic and rapidly changing clinical picture characterized by

delusions, hallucinations and mood disturbance, most commonly elation. A further four cases displayed an admixture of paranoia, grossly disorganized behavior, fleeting hallucinations and delusions and were diagnosed as mixed psychotic state. The latter diagnosis was made by a process of exclusion of other diagnostic subtypes. Significantly, there was no case of a predominantly depressive psychotic state

Psychotic disorders

**Psychotic disorders associated with cannabis use**
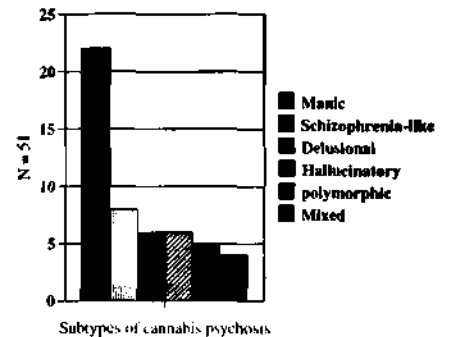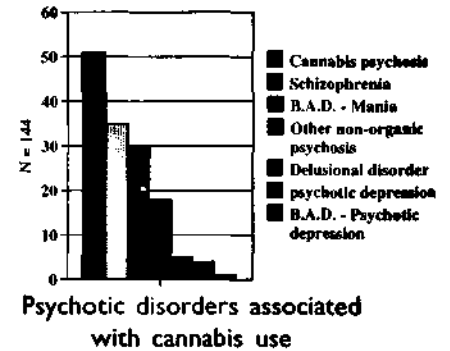
Subtypes of cannabis psychosis

that could be attributed to cannabis abuse. Twelve patients with cannabis psychosis had consumed substances other than cannabis including alcohol (10 cases) and two cases of polysubstance abuse/dependence. These were diagnosed as cannabis psychosis because of a temporal link between cannabis use and onset of psychosis.

Treatment given

About half the patients (49.5%) received antipsychotic medication (49.5%); twenty-three patients (9%) received a mood-stabilizing agent while 12 (%) were prescribed antidepressants.
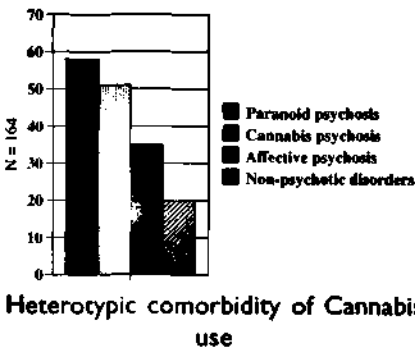
DISCUSSION

This study has a large patient sample of chronic and heavy cannabis users coming from a wide geographical catchment area including urban, peri-urban, sub-rural, and rural populations. The sample is representative of all strata of the society. The strengths of the study included data collected at an academic institute with a tradition of good record keeping and diagnostic coding. A manual search in addition to electronic search was carried out to locate all case-notes thereby minimizing the chances of missing cases. Down-rating the aetiological role of cannabis in favour of a functional diagnosis would have further reduced any spurious attribution of mental disorders solely to cannabis use.

a) Heterotypic Comorbidity

Our results suggest that heavy and chronic use of cannabis can both cause a cannabis-induced psychosis and be associated with functional psychoses. Broadly, the nature of psychosis associated with heavy cannabis use is non-specific in that it includes both paranoid and affective psychosis but also a polymorphic disorder that cannot be categorized within either of the two groups. A smaller proportion of patients also developed non-psychotic disorders. The presence of a wide variety of psychiatric disorders associated with cannabis abuse therefore confirmed the study hypothesis. The rate of psychiatric morbidity is comparable to earlier reports [Troisi et al 1998, Weller and Halikas 1985].

b) Cannabis and Manic Psychosis

The most significant finding of the study was the association of cannabis abuse with development of manic disorder. Whilst there are previous smaller reports of a possible association between cannabis use and mania, [Dhunjibhoy 1930, Rottanburg et al 1982, Carney et al 1984, Harding and Knight 1973] we believe that our study is the first one to confirm this relationship in a sizable number of patients. In our cohort, some patients with a past history of mania and cannabis abuse appeared to become

sensitized to the effects of cannabis over a period of time so that for subsequent episodes of mania there appeared to be a progressive decrease in the time gap between re-onset of cannabis use and onset of mania. In other words, the relative shortening of time to relapse following reintroduction of cannabis use in successive episodes in this select group of patients appeared analogous to the process of 'kindling' [Post et al 1989, Post et al 1982]. By 'hastening' manic relapses, cannabis appeared to act as a precipitant, akin to the "life-event stressor" first suggested as a triggering mechanism in cases of schizophrenia [Andreasson et al 1987]. The association between cannabis abuse and mania gains further support from a recent study wherein cannabis use during follow-up of 50 new-onset bipolar disorder patients was associated with the experience of mania, whilst alcohol abuse was linked to the experience of depression [Strakowski et al 2000].

There may be possible biological explanations for the association between cannabis abuse and mania. Delta-9-tetrahydrocannabinol (THC), the active ingredient of cannabis, produces euphoria [Brill and Nahas 1984]. Under laboratory conditions high doses of THC have been shown to produce visual and auditory hallucinations, delusions, thought disorder and symptoms of hypomania in normal volunteers [Georgotas and Zeidenberg 1979]. Recent evidence also suggests that cannabinoid receptors, especially CB-1, located in substantia nigra, hippocampus, cerebellum and striatum, may be neuromodulatory by decreasing the uptake of GABA and dopamine, thereby potentiating their actions [D'Souza and Kosten 2001]. Further prospective and case-control studies, which control for other substance misuse are needed to elucidate this further.

ii) Cannabis Psychosis

Our results suggest that besides the triggering effect of cannabis in established bipolar disorders, cannabis psychoses can also present as a manic episode. We also found other psychotic presentations

suggesting that cannabis psychosis can present as schizophrenia-like, predominantly delusional or hallucinatory, as affective psychosis or as a polymorphic and rapidly changing psychosis. We could not confirm the previous suggestions that the presence of confusional state is a hallmark of cannabis psychosis [Johns 2001, Chopra and Smith 1974, Chaudhry et al 1991, Tennant and Groesbeck 1972, Goel and D'Netto 1975] since only three patients in this study displayed a confusional state. The DCR position, which does not prioritize this particular feature to a position of primacy in making a diagnosis of cannabis psychosis, is therefore validated.

iii) Cannabis and Schizophrenic Psychosis

Our results confirm the association between cannabis abuse and paranoid psychoses, especially schizophrenia. However, even some of these cases have prominent affective features, consistent with previous reports [Thacore and Shukla 1976, Rottanburg et al 1982, Tsuang et al 1982]. In addition, in a substantial proportion of our cases, only a diagnosis of 'other non-organic psychotic disorders' (F29 category) [World Health Organization 1993a] could be made on account of bizarre symptomatology, particularly grossly disorganized behavior. Whilst the diagnosis of catatonic schizophrenia had been made for several of these patients by treating clinical teams, this diagnosis was found unsupported by DCR criteria, which specify that catatonic symptoms are not diagnostic of schizophrenia and may be provoked by other aetiologies including alcohol or drugs [World Health Organization 1993b].

b) Homotypic Comorbidity:

Cannabis has been known as a 'gateway drug', and recent evidence suggests that even after controlling for a wide range of known risk factors for illicit drug use, cannabis use is associated with an increased risk of progression to other illicit drug use [Fergusson and Horwood 2000]. Our study confirms this since many subjects had alcohol, opioid and polysubstance abuse

and dependence in this group. Cannabis was the first drug of use in the substance use life-trajectories of two-thirds of this population, the remaining third starting with alcohol or opioids. However, for two-thirds of the whole cohort cannabis remained the only drug of abuse. Whilst this may appear contradictory to the foregoing, we believe that it is not inconsistent for people to progress from cannabis use to other illicit drugs in experimental ways, but to continue to preferentially use cannabis in a dependant manner, thereby confirming that in countries such as India that have a tradition of cannabis use, the widespread use of other substances is limited [Basu et al 1994].

The study findings are limited by the cohort being exclusively male, the lack of corroborative urine samples, possible recall bias and under-reporting by patients and, lack of any structured assessments, leading to reliance on case-note data alone.

CONCLUSIONS

Chronic and heavy abuse of cannabis in hospital attending patients in India is associated with widespread psychiatric morbidity. The onset of cannabis use begins at a relatively early age and heralds the experimentation with other psychoactive drugs. For the majority, however, cannabis remains the only drug of abuse. Experience of a psychotic illness is one of the major adverse effects of heavy cannabis use, particularly in those that present to psychiatric hospitals. Whilst our study confirms some of the earlier findings of association of cannabis use and the development of cannabis psychosis and schizophrenia, most significantly it reveals that heavy cannabis use can specifically cause a mania-like psychosis and more generally act as a precipitant for manic relapse in bipolar patients.

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