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Cannabis involvement in individuals with Bipolar Disorder

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Abstract

In a study of 471 BD cases and 1761 controls, individuals with BD were 6.8 times more likely to report a lifetime history of cannabis use. Rates of DSM-IV cannabis use disorders in those with BD were 29.4% and were independently and significantly associated with increased suicide attempts, experience mixed episodes and disability attributable to BD.

Keywords

cannabis; bipolar disorder; comorbidity

1. INTRODUCTION

Bipolar Disorder and disorders of the Bipolar Spectrum (BD) are, globally, the sixth leading cause of disability (Woods, 2000). 20-50% of BD subjects endorse some form of cannabis-related problems (Cerullo and Strakowski, 2007) with a recent study reporting higher severity of illness and greater treatment non-compliance in chronic cannabis users (van, I et al. 2009). While there has been a considerable amount of interest – and controversy – surrounding the associations between cannabis use and (variously defined) “psychosis” (Hall and Degenhardt 2000; Macleod et al., 2007), a recent study shows only a modest reduction in the association between cannabis use and mania when excluding psychotic features (Henquet et al., 2006). However, prior studies that have examined the association between cannabis-related behaviors and BD are characterized by several limitations

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including low sample size, limited assessments of BD and also limited data on comorbid conditions. We (a) report on the association between lifetime cannabis use and BD; (b) examine patterns of cannabis involvement in those with BD and (c) investigate BD-related outcomes in those with comorbid cannabis use disorders.

2. METHODS AND MATERIALS

2.1. Subjects

Extensive information on ascertainment of cases and controls is available in a related publication (Smith et al., 2009). Briefly, cases were unrelated subjects diagnosed with DSM-IV BD 1 as well as a small subset with BD spectrum disorders, using best estimate diagnosis. We used data collected using the DIGS 4.0 (Nurnberger, Jr. et al., 1994) from 321 European-American and 150 African-American individuals. Controls were drawn from a larger pool of subjects from across the U.S. who agreed to donate a blood sample for transformation into lymphoblastoid cell lines and to respond to a medical questionnaire. Only individuals with complete or near-complete psychiatric questionnaire data who did not fulfill diagnostic criteria for major depression, and did not report a history of schizophrenia, bipolar disorder or psychosis were retained – further matching for gender and ethnicity with BD cases allowed for inclusion of 1081 European-American and 680 African-American subjects.

2.2. Measures

All BD, cannabis involvement and psychpathology measures were collected using the semi-structured DIGS 4.0. Best estimate diagnosis of DSM-IV (American Psychiatric Association, 1994) BD and BD spectrum disorders were used. 89.8% of the 471 cases, were diagnosed with Bipolar I, 6.7% with Schizoaffective, Bipolar, and the remainder with Bipolar II (with recurrent depression) or Bipolar NOS. While no adjustments were made for confidence associated with diagnosis, 80% of the subjects were diagnosed with definite diagnostic confidence with the remainder being diagnosed with a high level of confidence (only missing supporting observations). Diagnoses for comorbid DSM-IV psychiatric and substance use disorders were also extracted from the best estimate diagnosis section. Clinical features of BD were rated by a clinician, based on responses to a variety of questions in the DIGS as well as interviewer narratives. For instance, BD-related disability was rated by a clinician as follows: 0=never ill, 1=no loss of employment or marital status, 2= loss of status but not disabled, 3=disabled but lives independently, 4=disabled and not living independently. This rating was based on multiple interview items rating general impact of illness on life functioning (e.g. did something happen as a result of illness (such as marital separation, absence from work or school, loss of job, or lower grades) as well as interviewer observations and clinical overview of the complete interview.

Data on lifetime cannabis use was available on cases and controls. In the cases, subjects who reported a lifetime history of 21 or more instances of cannabis use in a single year were queried about their age at first cannabis use as well DSM-IV abuse criteria. Those endorsing a single abuse criterion were subsequently queried for the 6 DSM-IV dependence criteria as well as cannabis withdrawal. Age at meeting criteria for, and recency of, DSM-IV cannabis abuse/dependence were also available.

2.3. Statistics

To examine the association between cannabis use and abuse/dependence and aspects of BD, chi-square analysis of contingency tables was used along with logistic regression controlling for sex, age, ethnicity, comorbid substance use disorders and DSM-IV psychopathology.

3. RESULTS

Compared with controls, BD cases were 6.8 times [95% C.I. 5.41-8.52] more likely to report a lifetime history of cannabis use – 71.3% of the cases, compared with 26.8% of the controls. This association was not modified by sex (p=0.22), however, the association was somewhat less strong in African-American (O.R. 0.48, 95% C.I. 0.29-0.76) subjects and in those aged 18-34 years (O.R. 0.58, 0.34-0.98). The association between BD and lifetime cannabis use persisted even after adjusting for other forms of substance use (alcohol, nicotine, cocaine and other illicit drugs).

Characteristics of cannabis-related behaviors in individuals with BD are presented in Table 1. Fifty seven percent of users reported using cannabis 21 or more times in a single year. Rates of DSM-IV abuse/dependence were high – 30% of individuals with BD (72% of those reporting lifetime use of 21 or more times in a single year) met criteria for DSM-IV cannabis use disorders. Fifty-three percent of the cases reported onset of a mood episode (depression, mania or hypomania) prior to their onset of cannabis use – the onset of a manic/hypomanic episode prior to onset of cannabis use was more common (43%) than onset of a depressive episode prior to cannabis use (21%). Of those who had used cannabis 21 or more times in a single year, 45% met criteria for cannabis use disorders prior to, or concurrent with the onset of BD – manic/hypomanic episodes were more likely than depressive episodes to precede onset of cannabis use disorders.

In this sample, 64% of individuals with BD reported affective psychosis (during mania, depression or both). Of those with psychosis, 79.2% had experienced psychotic features during 2 or more episodes of depression or mania. The association between cannabis use disorders and BD was not attributable to psychosis nor to chronicity. Presence of psychosis was also not associated with lifetime cannabis use or with using cannabis for the first time prior to age 14 (early use).

In these data, those who initiated using cannabis prior to their first manic/hypomanic/depressive episode had a significantly lower mean age at first use (15.1 vs. 17.7 yrs) while those who used cannabis after (or in tandem with) their onset of a manic/hypomanic/depressive episode had a lower age at onset of BD (17.5 vs. 21.5 yrs). Those who used cannabis prior to onset of a BD episode were 1.75 [95% C.I. 1.05-2.91] times more likely to report disability attributable to BD. Thus, earlier onset of cannabis use was associated with BD-related disability.

Those meeting lifetime criteria for DSM-IV cannabis use disorders experienced greater disability – 63.7% of those with cannabis use disorders reported disability while only 44.5% of those not meeting criteria reported disability. Those individuals with BD who reported comorbid cannabis use disorders were 2.2 times more likely to report disability in life-functioning attributable to BD and also a modest increased probability of attempting suicide. Mixed episodes were more common in those with a lifetime history of DSM-IV cannabis use disorders. Importantly, even after controlling for all sociodemographic, substance use and psychiatric covariates, those with DSM-IV cannabis use disorders were 1.8 times more likely to report disability due to BD than those without a history of cannabis use disorders.

4. DISCUSSION

Cannabis use and use disorders are more common in those with BD and their presence is independently associated with greater disability associated with BD. This exacerbation of BD-related life functioning in those with cannabis abuse/dependence is independent of psychosis and other co-occurring psychopathology and substance use disorders. For individuals presenting with BD, efforts should be made both to assess their extent of

cannabis use and, for those presenting with problematic use, to reduce their levels of use. Whether such a reduction has a causal influence on the etiology of BD is speculative but evidence for better treatment outcomes in non-users does exist (Baethge et al., 2005).

Some caveats to this study are noteworthy. First, data on cannabis use disorders are not available in control subjects. Second, we elected to use data collected with the DIGS 4.0 as this provided the most comprehensive assessment and also excluded any heterogeneity attributable to assessment – thus, individuals assessed using prior versions of the DIGS were excluded. This did not influence the association between BD case status and cannabis use. Retaining only those subjects with a Bipolar I diagnosis also did not modify the association. Finally, the retrospective nature of the data precludes tests of causality.

In conclusion, there is ongoing debate on the efficacy of medication for BD in individuals afflicted with comorbid substance use disorders and on the modifying effects of antipsychotic medication on the endogenous cannabinoid system (Hamdani et al., 2008; Wiley et al., 2008; Leweke and Koethe, 2008). BD cases with comorbid cannabis use disorders are a vulnerable population and continued efforts to identify integrated treatments for dually diagnosed patients is vital.

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TABLE 1

Prevalence of cannabis involvement and prevalence of, and association between, DSM-IV cannabis use disorders and clinical features of Bipolar Disorder (BD) in 471 GAIN cases interviewed using DIGS 4.0.

	All cases
Lifetime use	71.3% (N=330)
21+ times in a single year	40% (N=186)
DSM-IV abuse/dependence	29.4% (N=138)
Mean age at 1st use	16.7 [7-45 years]
Mean age at DSM-IV cannabis use disorders	19.2 [12-36 years]
Mean age at recency of DSM-IV cannabis use disorders	29.8 [15-57 years]

	% in those with cannabis use disorders (N=138)	**% in those without cannabis use disorders (N=331)**	**O.R. [95% C.I.]**	**Multivariate O.R.* [95 % C.I.]**
Psychosis	62.3% (N=86)	64.7% (N=214)	0.90 [0.60-1.36]	ns
Rapid Cycling	24.6% (N=34)	27.2% (N=90)	0.88 [0.55-1.38]	ns
Mixed Episodes	53.6% (N=74)	43.2% (N=143)	1.52 [1.02-2.27]	1.44 [0.93-2.24]
Incapacitation during depression	83.3% (N=115)	82.8% (N=274)	1.04 [0.61-1.77]	ns
Incapacitation during mania	81.9% (N=113)	86.1% (N=285)	0.73 [0.43-1.24]	ns
General disability associated with life functioning (self-reported disabled, living independently or not)	63.7% (N=86)	44.5% (N=145)	2.19 [1.45-3.31]	**1.81 [1.13-2.91]**
Suicide attempt (self-reported – acted with ambivalence/intent to die with minimal/serious consequences)	60.9% (N=84)	50.8% (N=168)	1.51 [1.01-2.26]	1.33 [0.85-2.10]
Mean depression episodes	21.2	23.0	ns	ns
Mean mania episodes	14.6	13.7	ns	ns

* Only shown when univariate is significant. Covariates for multivariate analyses include age, sex, ethnicity, a variable representing DSM-IV abuse/dependence on alcohol or cocaine or sedatives, stimulants, opiates or other drugs or DSM-IV nicotine dependence and a variable representing meeting criteria for DSM-IV panic disorder with/without agoraphobia, agoraphobia without panic disorder, social phobia, specific phobia, obsessive compulsive disorder, anorexia nervosa, bulimia nervosa, pathological gambling, attention deficit hyperactivity disorder or antisocial personality disorder.

ns=not significant at $p < .05$