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Demographic and clinical characteristics associated with comorbid cannabis use disorders (CUDs) in hospitalized patients with bipolar I disorder

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Abstract

Background—Published data suggest that cannabis use is associated with several negative consequences for individuals with bipolar disorder (BD), including new manic episode onset, psychosis, and functional disability. Yet much less is known about cannabis use disorders (CUDs) in this population, especially in more acutely symptomatic groups.

Methods—To evaluate correlates of CUD comorbidity in BD, a retrospective chart review was conducted for 230 adult patients with bipolar I disorder (BDI) who were admitted to a university-affiliated private psychiatric hospital. Using a computer algorithm, a hospital administrator extracted relevant demographic and clinical data from the electronic medical record for analysis.

Results—Thirty-six (16%) had a comorbid CUD. CUD comorbidity was significantly associated with younger age, manic/mixed episode polarity, presence of psychotic features, and comorbid nicotine dependence, alcohol use disorder (AUD), and other substance use disorders, but was associated with decreased likelihood of anxiety disorder comorbidity. With the exception of manic/mixed polarity and AUD comorbidity, results from multivariate analyses controlling for the presence of other SUDs were consistent with univariate findings.

Conclusion—Patients with BD and comorbid CUDs appear to be a complex population with need for enhanced clinical monitoring. Given increasing public acceptance of cannabis use, and the limited availability of evidenced-based interventions targeted toward CUDs in BD, psychoeducation and other treatment development efforts appear to be warranted.

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Conflicts of Interest

The authors have no conflicts to declare.

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Keywords

bipolar disorder; cannabis use disorder; substance use; psychosis

1. Introduction

The elevated prevalence of substance misuse in bipolar disorder (BD) has been well documented [1], with evidence that rates of comorbid substance use disorders (SUDs) are among the highest in BD relative to the other major psychiatric disorders [2,3]. As in the general population, tobacco and alcohol represent the most widely abused substances in BD, with cannabis representing the most common illicit substance of abuse [2,4]. Rates of lifetime cannabis use have been reported in up to 64% of individuals with BD [5], and data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) [2] reveal a 12-month prevalence rate of 7.2% for cannabis use disorders (CUDs) among those with a lifetime BD diagnosis [6]. This figure represents a 6-fold increased risk for CUDs in BD compared to the general population estimate of 1.2%, and increased risk relative to the other major psychiatric disorders, with CUD comorbidity rates ranging from 2.9 – 5.7% [6,7]. Among those with a more recent history of bipolar disorder (i.e., 12-month diagnosis), CUD comorbidity has been reported to be even higher, with rates as high as 9.4% [7].

There is an emerging literature focused on the correlates of cannabis use in BD, with some evidence that cannabis users are more likely to be male, to abuse alcohol and other substances, to experience greater overall illness severity, and to evidence poorer treatment adherence when compared to non-users [8–10]. Particularly alarming, cannabis use in BD has also been associated with significantly increased risk for new onset [10–15] and longer duration [9,16,17] of manic episodes, as well as incidence of psychosis [8,10]. Data have also revealed a dose-response relationship between the degree of cannabis use and first onset of BD, with heavier users (i.e., > 10 times within one month lifetime) reporting significantly earlier age of disorder onset compared to non-users [18].

Despite the growing literature on cannabis use in BD, less is known about CUDs in this population, especially in more acutely ill samples. Within community samples, as in the general population, a 12-month CUD diagnosis within BD has been linked to male sex and younger age [6,7,19]. CUD comorbidity in BD has also been associated with earlier age of BD onset, more frequent mood cycling, and greater rates of comorbid other SUDs, including nicotine dependence, alcohol use disorders (AUDs), and non-cannabis drug use disorders [6]. Additional data reveal greater rates of disability [20] and poorer physical quality of life [6] in community samples of individuals with BD and comorbid CUDs, and some [20], but not all [6,21], have demonstrated elevated risk for suicide attempt among those with BD and a comorbid CUD.

Although informative at the population level, epidemiologic and other community studies may be limited in generalizability to the clinical setting. Yet within clinical samples, there is limited research focused on CUD comorbidity in BD. Among the few published studies within patient populations, results support associations between CUD comorbidity and male sex [17,22] and increased incidence of psychosis [17,22]. However, these studies have relied

upon primarily manic [17] or mixed euthymic and symptomatic [22] samples, thus limiting an ability to evaluate features that may be more relevant to acute bipolar depression, in particular. Building upon this growing literature, the aim of this exploratory study was to further advance an understanding of CUD comorbidity in BD, utilizing a sample of acutely ill patients with bipolar I disorder (BDI) presenting for psychiatric hospitalization. Use of this sample allowed for the evaluation of demographic and clinical correlates of CUD diagnosis within the context of routine clinical care, and across the full spectrum of BD mood symptomatology (i.e., current manic and depressive symptomatology).

2. Method

2.1. Participants

A retrospective chart review was conducted for patients with BDI admitted to the inpatient or partial hospitalization programs at Butler Hospital in Providence, RI, USA during the 2010 calendar year [23]. To be considered eligible for inclusion, patients must have been 18 years or older and given a primary diagnosis of BDI at both hospital admission and discharge. There were no other study inclusion criteria. For those patients with more than one hospitalization during this time period, we selected the first hospitalization within the calendar year as the index hospitalization. The resulting sample included 230 cases for analysis. Prior to initiating the study, a Protected Health Information waiver and approval to conduct the chart review were obtained from the Butler Hospital IRB.

2.2. Procedure

Relevant demographic and clinical information was extracted from electronic medical records by a hospital administrator and provided to the study first author in a single Microsoft Excel file. Using standard form fields from the hospital admission report, the hospital administrator used a computer algorithm to extract the following data: patient age, sex, race, ethnicity, civil status, history of prior psychiatric hospitalization, type of index hospitalization (i.e., inpatient vs. partial), self-reported pharmacotherapy for BD at hospital admission (i.e., yes/no), history of suicide attempt, and global assessment of functioning (GAF). DSM-IV-TR diagnostic codes were extracted from the admission and discharge reports in order to confirm the presence of a BDI diagnosis, and were further quantified into the following variables: polarity of BD mood episode (depressive vs. manic/mixed), presence of psychotic features (e.g., hallucinations and/or delusions) at hospital admission, and presence of any current anxiety disorder, cannabis use disorder (CUD), nicotine dependence, alcohol use disorder (AUD), or any other substance use disorder (SUD). ICD diagnostic codes, also extracted from the discharge report, were used to establish the presence of any comorbid medical condition. All diagnoses were made by attending psychiatrists within the context of routine clinical care. Categorical variables were dummy coded (0 = absent, 1 = present) by the study research assistant and checked for errors by the study first author prior to being imported into SPSS v.22 for analysis.

2.3. Data analysis

Consistent with the DSM-IV-TR diagnostic structure and coding, descriptive data for overall prevalence rates of comorbid cannabis abuse and dependence in the study sample were first

evaluated. All subsequent study analyses utilized a composite variable representing the presence vs. absence of any CUD, to be consistent with the existing literature [6,7,19,20] and recent collapsing of substance abuse and dependence diagnoses into singular substance use disorders in DSM-5. Independent *t*-test and chi-square analyses were used to evaluate demographic and clinical differences between patients with a CUD and those without. For any significant differences identified in the univariate analyses, multivariate logistic regression analyses were used to evaluate which characteristics remained significantly associated with a comorbid CUD diagnosis, controlling for the presence of other SUDs. Within these multivariate models, the presence of AUDs and nicotine dependence were combined with non-cannabis drug use disorders in the coding of other comorbid SUDs, with the exception of when they were evaluated as separate independent variables in their respective multivariate models. Thus, multivariate analyses allowed for the evaluation of the unique associations between patient characteristics and CUDs, over and above the variance accounted for by SUDs more generally. As this was an exploratory analysis, *p*-values were set at 0.05.

3. Results

3.1. Participant characteristics

The overall sample included 230 adults with BDI ranging in age from 18 to 77 (mean 42.2; *sd* = 12.6). Slightly more than half (*n* = 134; 58%) were female, and the majority were from White (*n* = 217; 94%), Non-Hispanic (*n* = 210; 91%) backgrounds. With respect to relationship status, 97 (42%) were single, never married, 61 (27%) were married or cohabiting, and 72 (31%) were divorced, separated, or widowed. One-hundred and forty (61%) were in a manic or mixed episode at the time of hospitalization and 85 (37%) were diagnosed as being in a major depressive episode. Episode polarity was not specified for the remaining 5 (2%) patients. Average GAF ranged from 15 – 65 (mean 46.7; *sd* = 9.7). Most patients (*n* = 163; 71%) had been hospitalized on an inpatient (vs. partial hospitalization) basis, and 185 (80%) had a documented history of prior psychiatric hospitalization.

3.2. Univariate results

In the overall sample, 24 (10.4%) had a diagnosis of cannabis abuse and 12 (5.3%) had a diagnosis of cannabis dependence. Altogether, 36 (15.7%) had a documented CUD diagnosis. Results from independent *t*-test and chi-square analyses, comparing those with and without a CUD diagnosis, are presented in Table 1. Overall, data revealed that those with a CUD diagnosis were significantly younger, more likely to be in a manic/mixed episode at the time of hospitalization, to present with psychosis, and to have additional comorbid diagnoses of nicotine dependence, AUD, and other SUDs. Those with comorbid CUDs were significantly less likely to have an anxiety disorder diagnosis at the time of hospital admission.

3.2. Multivariate results

Results from multivariate analyses, controlling for the presence of other comorbid SUDs, are presented in Table 2. These analyses revealed that CUD comorbidity in BD remained significantly associated with presence of psychosis and nicotine dependence, as well as a

lower likelihood of an anxiety disorder diagnosis at the time of hospital admission. Over and above shared variance with comorbid other SUDs, there was no longer a significant association between CUD comorbidity and mood episode polarity or presence of an AUD.

4. Discussion

With a prevalence of roughly 16%, study results revealed relatively high rates of current CUDs in hospitalized patients with BDI, surpassing the 9.4% rate reported in community samples of individuals with BD [6,7], but well within the range reported in other clinical samples of patients with BD [8,17,22]. Moreover, there was evidence for high clinical burden associated with CUDs in this otherwise acute sample of patients with BDI. Indeed, those with a comorbid CUD were significantly more likely to present with psychotic features, manic/mixed episode polarity, and comorbid nicotine, alcohol and non-cannabis drug use disorders. These data are highly consistent with findings reported in the broader cannabis use literature within BD [6,8,11,17] and further underscore the importance of careful monitoring of patients with BD and CUD comorbidity across clinical settings.

Accounting for the shared variance between CUDs and other SUDs, there remained significant associations between CUD comorbidity and psychosis and nicotine dependence, suggesting that these clinical features may represent more robust and unique correlates of CUD comorbidity in BD. In contrast, non-significant results from the multivariate models suggested that associations between CUD comorbidity and manic/mixed symptom polarity may be better accounted for by more general substance use behaviors that frequently co-occur with CUDs, and that shared variance with other comorbid SUDs may also better explain the associations between CUD comorbidity and greater likelihood of AUDs in BD. To our knowledge, this is the first study to demonstrate such effects, and will therefore require replication in other samples.

In addition to the clinical correlates described above, study data replicated prior findings that younger age is also associated with CUD comorbidity in BD [6]. However, inconsistent with some prior research in BD samples [6,7,19,20], there was no evidence in the current study for significant associations between CUD comorbidity and male sex, marital status, or functional impairment, as measured by GAF rating. These inconsistent findings may in part be a function of the acutely ill patient sample employed in the current study, wherein a more restricted range of illness severity may have impacted an ability to detect differences across demographic and functioning (i.e., GAF) measures. Similarly, we failed to demonstrate a significant association between CUD comorbidity and suicide attempt history in the current sample, which is consistent with prior research that has failed to establish this association within other BD samples [6,21] but may also be a function of the clinical acuity of the study sample as a whole.

Somewhat unexpectedly, current study data revealed that BD patients with CUD comorbidity were significantly less likely to present with an anxiety disorder at the time of hospital admission. These data directly contrast with prior research demonstrating significant associations between CUDs and anxiety disorders in general community samples [24,25]. Although it is possible that the nature or the direction of these associations may be

different among patients with BD, it is also possible that, as a function of its potential short-term, time-limited anxiolytic effects for some patients [26], active cannabis use may have masked underlying anxiety symptoms when patients presented for treatment. Further, given that these data were collected within the context of an acute clinical service where clinicians may not have had sufficient time to fully assess or detect the presence of lifetime disorders, it is likely that the majority of chart diagnoses evaluated in the current study were based upon point versus lifetime prevalence. As such, positive associations between lifetime CUD comorbidity and anxiety disorders, as has been demonstrated in prior research [24,25,27], may have been more difficult to detect in the current sample. The reliance upon point prevalence diagnoses may have also influenced null findings reported above (i.e., for suicide attempt history). Future research will be necessary in order to better clarify the associations between cannabis use and anxiety in patients with BD.

Future research will also be necessary to address other limitations of the current study. As noted above, the study relied upon retrospective chart review, which benefits from data collected within the context of routine clinical care, but also has a number of limitations. Although we were conservative in selecting those cases that had a BDI diagnosis at both admission and discharge, thereby reducing the heterogeneity of the sample, chart diagnoses were not confirmed by structured interview and secondary conditions (including SUDs) may not have always been assessed or documented in the electronic medical record. As a retrospective chart review, choice of demographic and clinical variables to evaluate in the current study was limited to what was available in the hospital admission report. As such, we were unable to evaluate associations between CUD comorbidity and certain relevant core features of BD such as age of onset [10,18], overall illness severity [6,20,28], history of mixed episodes [27] and rapid cycling [6,17], history of early adversity or trauma [29], current psychotherapy and pharmacotherapy treatment history and adherence [8,9], as well as other relevant features such as obesity and body mass index [30]. Further, study analyses were cross-sectional, and we were therefore unable to evaluate directionality of associations between CUD comorbidity and clinical and demographic features in the study sample. Finally, the study sample was primarily White and non-Hispanic. Thus, generalizability to more diverse patient groups with BD requires further study. Generalizability to patients with bipolar II disorder also requires further study.

In conclusion, current study data yield important descriptive information that adds to the growing literature on CUD comorbidity in BD, and highlight the corresponding high clinical burden associated with CUDs, especially within more acutely symptomatic patients with BD. Given increasing acceptance of cannabis use among legislators and the public [31], and evidence from prospective studies suggesting that CUD comorbidity further complicates long-term outcomes and BD treatment response [28,32], enhanced psychoeducation and other treatment development efforts appear to be warranted.

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Highlights

- Cannabis use disorders (CUDs) are linked to high clinical burden in bipolar disorder
- Data revealed unique associations between CUDs, psychosis and nicotine dependence
- Risk for anxiety disorders was lower among those with CUD comorbidity
- Enhanced clinical monitoring of CUDs in bipolar disorder appears to be indicated

Table 1

Characteristics associated with comorbid cannabis use disorder (CUD) in bipolar disorder: Univariate findings

	CUD (<i>n</i> = 36; 16%)	No CUD (<i>n</i> = 194; 84%)		
	<i>M</i> (<i>SD</i>) or <i>n</i> (%)	<i>M</i> (<i>SD</i>) or <i>n</i> (%)	χ^2	<i>p</i>
Age	38.4 (10.6)	42.9 (12.9)	1.95 [†]	0.053
Sex (female)	18 (50)	116 (60)	0.86	0.355
Race (White)	34 (94)	183 (94)	0.14	0.711
Ethnicity (Non-Hispanic)	32 (89)	133 (92)	1.14	0.287
Civil status			1.43	0.488
Single, never married	18 (50)	79 (41)	--	--
Married/cohabiting	7 (19)	54 (28)	--	--
Divorced/separated/widowed	11 (31)	61 (31)	--	--
Mood episode (manic/mixed)	27 (75)	113 (58)	3.93	0.048
GAF at admission	47.2 (8.0)	46.3 (10.0)	-0.48 [†]	0.635
Index hospitalization (inpatient)	26 (68)	137 (71)	0.04	0.846
History of previous hospitalization	32 (89)	153 (79)	1.94	0.164
Psychosis at admission	24 (67)	81 (42)	7.99	0.005
History of suicide attempt	13 (36)	88 (45)	1.89	0.169
Comorbid anxiety disorder	5 (14)	71 (37)	7.08	0.008
Comorbid AUD	13 (36)	38 (20)	4.80	0.028
Comorbid nicotine dependence	20 (56)	60 (31)	8.12	0.004
Comorbid other SUD	11 (31)	26 (13)	6.62	0.010
Any medical comorbidity	22 (61)	137 (71)	1.29	0.257
Any pharmacotherapy for BD at admission	28 (78)	158 (81)	0.26	0.608

Note. GAF = global assessment of functioning; AUD = alcohol use disorder; SUD = substance use disorder.

[†]For purposes of comparison of continuous data, t-tests were employed.

Characteristics associated with comorbid cannabis use disorder (CUD) in bipolar disorder: Multivariate findings controlling for the presence of a concurrent other substance use disorder (SUD)

Table 2

Logistic Regression Analyses	<i>B</i> (<i>SE</i>)	χ^2	<i>p</i>	OR	95% CI
Age	−0.04 (0.02)	4.37	0.036	0.97	0.93 – 1.00
Mood episode (manic/mixed)	0.73 (0.44)	2.73	0.098	2.08	0.87 – 4.96
Psychosis at admission	1.01 (0.41)	6.17	0.013	2.75	1.24 – 6.11
Comorbid anxiety disorder	−1.20 (0.51)	5.48	0.019	0.13	0.11 – 0.82
Comorbid AUD	0.65 (0.42)	2.40	0.121	1.92	0.84 – 4.36
Comorbid nicotine dependence	0.84 (0.39)	4.68	0.030	2.31	1.08 – 4.94

Note. AUD = alcohol use disorder; CI = confidence interval.