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Substance Use Disorders and Suicide Attempts in Bipolar Subtypes

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1. Abstract

Bipolar disorder (BD) is associated with high rates of suicide attempt and completion. Substance use disorders (SUD) have been identified as potent risk factors for suicidal behavior in BD. However, little is known concerning differences between BD subtypes with regard to SUD as a risk factor for suicidal behavior. We studied previous suicidal behavior in adults with a major depressive episode in context of BD type I (BD-I; N=96) or BD type II (BD-II; N=42), with and without history of SUD. Logistic regressions assessed the association between SUD and suicide attempt history by BD type, and exploratory analyses examined the effects of other clinical characteristics on these relationships. SUD were associated with suicide attempt in BD-I but not BD-II, an effect not attributable to sample size differences. The higher suicide attempt rate associated with alcoholism in BD-I was mostly explained by higher aggression scores, and earlier age of BD onset increased the likelihood that alcohol use disorder would be associated with suicide attempt(s). The higher suicide attempt rate associated with other drug use disorders in BD-I was collectively explained by higher impulsivity, hostility, and aggression scores. The presence of both alcohol and drug use disorders increased odds of a history of suicide attempt in a multiplicative fashion: 97% of BD-I who had both comorbid drug and alcohol use disorders had made a suicide attempt. A critical next question is how to target SUD and aggressive traits for prevention of suicidal behavior in BD-I.

Keywords

Bipolar disorder; suicide; risk factors; substance abuse; alcohol

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1. Introduction

Frequency of attempted suicide in Bipolar Disorder (BD) is among the highest of any mental disorders, both in the community (Chen & Dilsaver, 1996; Kessler et al., 1999; Szadoczky et al., 2000), and in clinical samples (Balazs et al., 2003; Bottlender et al., 2000; Cassano et al., 1992; Coryell et al., 1987; Endicott et al., 1985; Kupfer et al., 1988; Lester, 1993; Roy, 1993; Serretti et al., 2002). Between 25% and 60% of bipolar patients will attempt suicide during the course of the illness (Chen & Dilsaver, 1996; Goodwin & Jamison, 1990), and BD lifetime suicide completion rates are estimated at 14% to 20% (Axelsson & Lagerkvist-Briggs, 1992; Goodwin & Jamison, 1990; Guze & Robins, 1970).

A history of substance use disorders has been linked to suicide attempt risk in BD (Comtois et al., 2004; Dalton et al., 2003; Feinman & Dunner, 1996; Lopez et al., 2001; Potash et al., 2000; Tondo et al., 1999; Weiss et al., 2005). However, little is known about differences between BD-I and BD-II with regard to this suicide attempt risk factor. We therefore examined differences between BD-I and BD-II in associations between substance use disorders and history of suicide attempt. A secondary goal was to evaluate clinical factors modifying identified risk characteristics.

2. Methods

2.1 Subjects

Subjects (N=138) with a BD were recruited from community referrals or advertisements and enrolled in studies at two sites: the New York State Psychiatric Institute, New York (N=120), and the Western Psychiatric Institute and Clinic, Pittsburgh (N=18). All subjects gave written informed consent for participation after the nature of the procedures had been fully explained, as approved by the respective Institutional Review Boards. The primary inclusion criterion was a current major depressive episode in context of BD-I (N=96) or BD-II (N=42). We assessed for history of any SUD but did not distinguish between present or past SUD at time of presentation for purposes of this analysis.

2.2 Assessments

A psychiatric history, physical examination, and routine laboratory screening were performed. Diagnoses were made by trained master's level psychologists or psychiatric nurses using the Structured Clinical Interview I (SCID-I) for DSM IV Axis I disorders (American Psychiatric Association, 1994; First et al., 1997).

The sample was extensively characterized with regard to demographic and clinical characteristics. Axis II conditions were assessed using the Structured Clinical Interview II (SCID-II) for Axis II disorders. (American Psychiatric Association, 1987; First et al., 1995) Current depression severity was measured by the 17-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1967) and the Beck Depression Inventory (BDI) (Beck et al., 1961). Severity of suicidal ideation was rated for all subjects using the Scale for Suicidal Ideation (SSI) (Beck et al., 1979). The Reasons for Living Inventory was used to assess possible protective factors (Linehan et al., 1983). Lifetime aggression, impulsivity, and hostility were assessed with a modified form of the Brown-Goodwin Aggression History Scale (B-G) (Brown et al., 1979), the Barratt Impulsiveness Scale (BIS) (Barratt, 1965), and the Buss-Durkee Hostility Inventory (B-D) (Buss & Durkee, 1957), respectively. History of suicide attempts was assessed with the Columbia Suicide History Scale (Oquendo et al., 2003). Overall level of functioning was rated using the Global Assessment Scale. (Endicott et al., 1976) Some of the subjects included in this study have been included in previous analyses (Grunebaum et al.,

2006b; Harkavy-Friedman et al., 2006; Oquendo et al., 2004; Oquendo et al., 2000; Sher et al., 2006; Zalsman et al., 2006).

2.3 Statistical Methods

The two BD subtypes were compared in terms of demographic and clinical characteristics, using independent t-tests or Mann-Whitney U-tests for continuous variables and χ^2 tests for dichotomous variables, $\alpha = 0.05$.

To study whether associations between SUD and suicide attempt history differed between BD-I and BD-II groups, we performed separate logistic regression analyses with history of alcohol use disorder or drug use disorder as independent variables, diagnosis as cofactor, and attempter status as response variable; and we tested for interactions. As a check for effects of sample bias, the analyses were repeated, including as cofactor the characteristics with different distributions between BD-I and BD-II samples.

Within the diagnostic subgroup in which SUD were associated with history of suicide attempt, we performed additional analyses to ascertain whether the association could be explained in part by other demographic and clinical variables (listed in Table 1). In separate analyses, we compared subjects within one diagnostic group, with and without alcohol or drug use disorders, with regard to each variable, using independent t-tests or Mann-Whitney U-tests for continuous variables and χ^2 tests for dichotomous variables. Each SUD-associated factor and its significantly associated variables were then entered into separate logistic regression models, with prior suicide attempter status as outcome variable, and testing for interactions. Continuous covariates were centered.

3. Results

3.1 Overall comparisons between diagnostic groups

With regard to demographic and clinical characteristics, BD-I differed from BD-II only in a lower percentage of white subjects and a lower GAS score; a trend was seen toward a higher rate of reported physical/sexual abuse in BD-I (see Table 1). Samples at the two sites were not different with regard to diagnosis or attempter status distributions (data not shown).

3.2 Differences between BD-I and BD-II with regard to the association between SUD and suicide attempt history

As expected, both SUD and suicide attempts were frequent in this population (see Table 2). Rates of drug or alcohol use disorder did not differ between BD-I and BD-II samples; nor did numbers of subjects who had attempted suicide. However, logistic regression analyses revealed that in BD-I but not BD-II, a history of either drug or alcohol use disorders was associated with suicide attempt (see Table 3). This result remained significant when race, GAS scores, and reported history of physical/sexual abuse (factors that were or tended to be differently distributed between BD-I and BD-II in our sample), were included in the logistic regression model (data not shown). The lack of association between SUD and suicide attempt in BD-II did not appear to be a function of low statistical power due to small BD-II sample size. This is expressed by low odds ratios for drug or alcohol use and suicide attempt history within BD-II (alcohol use: $\chi^2=0.238$, $df=1$, $p=0.626$, $OR=0.714$, 95% $CI=0.185$ to 2.762 ; drug use: $\chi^2=0.626$, $df=1$, $p=0.429$, $OR=0.579$, 95% $CI=0.150$ to 2.241). Within BD-I, history of suicide attempt was *higher* among subjects with SUD compared to those without, whereas within BD-II, the attempt rate was *lower* in subjects with SUD compared to those without. This difference between the proportion of suicide attempters among those with SUD is significant in BD-I vs BD-II (see Table 2 of summary statistics, *No.(%) of Suicide Attempters/SUD Subjects*).

3.3 Features of the association between SUD and suicide attempt within BD-I

There was considerable overlap between alcohol and drug use disorders among subjects with BD-I: 31% of subjects had a history of both types of disorders. In separate logistic regression analyses, suicide attempt status was associated with both alcohol use disorder ($\chi^2=6.23$, $df=1$, $p=0.013$, $OR=4.07$, 95% $CI=1.35$ to 12.27) and drug use disorder ($\chi^2=7.92$, $df=1$, $p=0.005$, $OR=6.5$, 95% $CI=1.77$ to 23.9). When the contributions of each type of disorder to suicide attempt were examined in a combined model, a larger portion of the odds was explained by drug use disorder ($\chi^2=4.96$, $df=1$, $p=0.026$, $OR=4.70$, 95% $CI=1.20$ to 18.32) than by alcohol use disorder ($\chi^2=2.42$, $df=1$, $p=0.120$, $OR=2.54$, 95% $CI=0.78$ to 8.23). This model is additive because the interaction term between the two factors was not significant, and thus the predicted combined OR in the situation of both risk factors (drug and alcohol use disorders) is calculated by multiplying the odds ratios ($2.54 \times 4.70 = 11.9$). When a history of both types of SUD was included as the independent variable in logistic regression analysis, the observed OR was 12.6 ($\chi^2=11.1$, $df=1$, $p=0.001$, $OR=2.54$, 95% $CI=1.61$ to 99.07). Among BD-I subjects who had a history of both alcohol and drug use disorders ($N=29$), 97% had made at least one suicide attempt.

3.4 Exploratory analyses of the effects of other variables on the association between substance use disorders and past suicide attempt in BD-I

As described in detail in Statistical Methods, in order to understand differences between bipolar subtypes in effects of SUD on suicide attempt, we performed analyses *within each bipolar subtype*, to identify SUD-associated factors. Logistic regression models were then performed with SUD-associated factors as independent variables and prior suicide attempter status as outcome variable, and testing for interactions. The purpose of these analyses was to test whether other factors may have influenced the relationship between SUD and suicide attempt. We note that these analyses are exploratory in nature and serve primarily to suggest future avenues for prospective research.

Variables found to be associated with drug use in BD-I were traits of aggressivity, impulsivity and hostility, age of onset of bipolar illness, severity of depression on HDRS, number of major depressive episodes, smoking, and family history of suicidal behavior. Among these variables, we found that the odds ratio for prior suicide attempt in drug use disorder ($OR=6.50$, 95% $CI=1.76$ to 23.93 , $p=0.005$) was significantly affected by only three variables: aggression (reduced OR to 2.78, 95% $CI=0.63$ to 12.27 , $p=0.177$); impulsivity (reduced OR to 3.20, 95% $CI=0.78$ to 13.12 , $p=0.106$); and hostility (reduced OR to 3.67, 95% $CI=0.84$ to 16.12 , $p=0.0858$); and there were no interactions. Reduction of the odds ratio indicates that these variables explain a significant portion of the relationship between drug use disorder and prior suicide attempt, and thus might be considered mediators. Given that these variables were highly correlated (aggression-impulsivity, Pearson's $r=0.461$, $p<0.001$; aggression-hostility, Pearson's $r=0.593$, $p<0.001$; impulsivity-hostility, Pearson's $r=0.560$, $p<0.001$), a principal component analysis was conducted, and 3 factors emerged. The first factor, Factor 1, explained 71% of the variance; when Factor 1 was entered into a final logistic regression model together with drug use, the odds ratio for drug use was somewhat reduced (drug use $OR=3.84$, 95% $CI=0.93$ to 15.89 , $p=0.06$). Factor 1 corresponds to the aggression/impulsivity factor previously identified by us, in a larger sample that included subjects with Major Depressive Disorder and BD ($N=308$), as increasing risk of future suicide attempts. (Oquendo et al., 2004)

Variables associated with alcohol use disorders in BD-I were aggression, earlier age of onset of bipolar illness, smoking, and physical/sexual abuse. Considering these variables, we found that aggression explained a significant portion of the relationship between alcohol use disorders and previous suicide attempt, as the odds ratio for the alcohol use disorder/suicide attempt relationship ($OR=4.07$, 95% $CI=1.35$ to 12.27 , $p=0.013$) lost significance when adjusted for

aggression (alcohol use OR=2.26, 95% CI = 0.69 to 7.39, $p=0.179$), without interactions. Age of bipolar illness onset as an additive factor only slightly modified the odds ratio (reduction of alcohol use OR to 3.21, $p=0.068$, 95% CI = 0.92 to 11.20), but exhibited a significant interaction with alcohol use disorder ($\chi^2=4.68$, $df=1$, $p=0.031$, OR=0.81, 95% CI= 0.644 to 1.02), and thus might be a moderator of the relationship between alcohol use disorder and suicide attempts. That is, an earlier bipolar disorder onset—whether depression or mania—further increased the chance that a subject with alcohol use disorder would also have made a suicide attempt(s), but the same was not true for subjects without the alcohol use disorder. To ascertain that the effect of age of onset was not merely a surrogate for how long the subject had been ill, we repeated the analysis with length of illness instead of age of onset as the additive variable; no significant effect was seen on the OR for the alcohol use disorder/suicide attempt relationship nor was any interaction with alcohol use disorder found (data not shown).

3.5 Exploratory analyses of the effects of aggression, suicide attempts, substance use disorders and past suicide attempt in BD-II

In order to better understand the lack of effect of SUD in BD-II, we also performed exploratory analyses concerning the relationships between aggression, suicide attempts, and SUD within that subgroup. We found that although higher aggression was associated with suicidal behavior ($t=2.67$, $df=40$, $p=0.011$) and substance use disorder was associated with higher aggression (alcohol: $t=3.48$, $df=38$, $p=0.001$; drugs: $t=2.48$, $df=38$, $p=0.018$), substance use disorder was not associated with suicidal behavior (alcohol: $\chi^2=0.34$, $df=1$, $p=0.558$; drugs: $\chi^2=0.76$, $df=1$, $p=0.383$).

4. Discussion

4.1 Suicide attempt risk and substance use disorders among Bipolar subtypes

The relative risk of suicide attempt and completion between subtypes of BD is unclear. Several studies suggest that Bipolar Disorder Type II (BD-II) has higher potential for suicide attempts (Allilaire et al., 2001; Bulik et al., 1990; Dunner et al., 1976; Goldring & Fieve, 1984; Serretti et al., 2002; Stallone et al., 1980) than other mood disorders. However, others have found no differences between Bipolar Disorder Type I (BD-I) and BD-II in suicide attempt (Coryell et al., 1989; Endicott et al., 1985; Leverich et al., 2003; Slama et al., 2004; Vieta et al., 1997) rates. A couple of reports found more suicide attempts in BD-I than BD-II (Cassano et al., 1992; Coryell et al., 1987). SUD have been found to occur at similar rates in BD-I and BD-II (Tondo et al., 1999; Weiss et al., 2005). In this study, rates of suicide attempts as well as substance use disorders were similar in both BD conditions (see Table 1).

Despite these similarities, SUD emerged as BD-I-specific correlates for suicide attempt. (Tondo et al., 1999; Weiss et al., 2005). The overwhelming majority of our subjects with BD-I with drug (93%), alcohol (89%), or combined substance (97%) use disorders made attempts. If confirmed in larger, prospective studies, this magnitude of effect provides clinically useful knowledge to guide decision making, such as whether to hospitalize a possibly suicidal patient. Obviously these findings merely explain a portion of the risk, as only slightly greater than half the BD I suicide attempters had a drug (52%) or alcohol (56%) use problem, and BD I subjects in this study without substance use disorders also had high rates of suicide attempt (67%).

As evidenced by the parameter estimates, the absence of an effect of substance use disorders on suicide attempt status in BD-II was not due to lack of statistical power resulting from sample size differences. Thus, we reasoned that some additional, BD-I-specific factors appear to be involved in effects of substance use disorders on suicide attempt risk.

4.2 Aggressive-impulsive traits as possible mediators of the association between substance use disorders and suicide attempts in BD-I

We have previously reported on analyses with different objectives that share some subjects with the current study, our findings that bipolar suicide attempters exhibited pronounced aggression (Oquendo et al., 2004; Oquendo et al., 2000), impulsivity (Oquendo et al., 2004), and hostility (Galfalvy et al., 2006); that aggression was associated with past (Zalsman et al., 2006) and subsequent (Sher et al., 2006) suicide attempts; and that SUD in BD have been associated with both impulsive-aggressive traits and number of suicide attempts (Grunebaum et al., 2006a). Other groups have likewise found that aggression was associated with suicidal threats (Papoulos et al., 2005) in BD, and that trait impulsivity increased additively in BD comorbid with substance abuse (Swann et al., 2004). In the present analysis, these same traits partly explained the association of prior suicide attempt to SUD, specifically in BD-I. The lack of interactions between SUD and aggressive-impulsive traits suggests that these traits may be partial mediators of the SUD effects on suicide attempt risk (see Figure 1). We thus speculate that the combination of SUD and BD-I symptoms may foster aggression, impulsivity, and hostility that increase the chances of acting on suicidal thoughts. Based on our retrospective data, however, it is not possible to know the temporal relationships between depression, mania, drug use, and suicide attempt. Thus, prospective studies would be needed to determine whether these traits are mediators of SUD effects on suicide attempt. Another difficulty in understanding the precise role of aggression, hostility, and impulsivity in suicide attempts among BD patients is that ‘trait’ and ‘state’ attributes are not always easily separable, as many individuals may spend the majority of their lives at least partially symptomatic (Judd et al., 2002).

In BD-II, although SUD was associated with higher aggression, and aggression with suicidal behavior, SUD was not associated with suicidal behavior. Therefore in this diagnostic group, aggression was associated with suicide attempt risk independently of SUD. Our data do not provide a direct explanation for the surprising difference in the association between SUD and suicide attempt between BD-I and BD-II. However, since the cardinal clinical factor distinguishing between the two conditions is the severity of the manic phase, one hypothesis is that excessive use of drugs or alcohol may lead to dysphoric manic or mixed states. Among subjects with BD-I onset prior to development of SUD, the percentage of time with SUD has been associated with the amount of time in mixed episode. (Strakowski et al., 2005) There is previous evidence linking dysphoric mania (Goldberg et al., 1999) and/or mixed states (Balazs et al., 2006; Goldberg & McElroy, 2007) both with substance disorders and with suicidal ideation and violent behaviors. However, our data do not include specific information on mixed or dysphoric manic states, nor on temporal relationship between BD-I or SUD onset.

4.3 Other possible explanations for the association of substance use disorders and suicide attempts in BD-I

Another hypothesis would posit BD-I as a more severe illness overall than BD-II, with more profound effects on a person’s ability to function successfully in school, social, and work environments, although it is unclear how that would lead to an association between SUD and suicide attempt. Psychosocial functioning is a complex outcome measure that has been found to be significantly impaired in both BD-I and BD-II, more intensively studied in the former condition (reviewed in (Huxley & Baldessarini, 2007)). In the 15-year longitudinal National Institute of Mental Health Collaborative Depression Study, subjects with BD-I were found to have more functional disability than those with BD-II (Judd et al., 2008). For each level of depression severity, however, BD-I and BII had an equal level of impairment. (Judd et al., 2005) Perhaps related to our hypothesis, manic symptom severity was associated with functional impairment, but in BD-II subjects, hypomanic symptom severity was associated with no impairment or even functional improvement (in the case of subsyndromal hypomania). (Judd et al., 2005) In our sample, we found the global functioning (GAS) to be lower in BD-I

group, with, however, no differences between diagnostic groups in other measures of illness severity and/or functioning, including depression severity as measured by HDRS scores, education, income levels, and rates of substance use disorders.

Other mechanisms for the relationship of substance use disorders to suicidality in BD have been proposed. For instance, genetic factors could account for the association: BD, alcoholism, and attempted suicide cluster in some families identified through a BD-I proband (Potash et al., 2000). The increased suicide risk could also arise from additional neurobiological factor (s) that have associations with both substance use disorders and bipolar disorder. For example, abnormal serotonin function has been linked to suicide risk (Mann, 1998), lifetime severity of aggressivity (Placidi et al., 2001), and bipolar disorder (Cannon et al., 2006). In preclinical studies, alcohol consumption has also been linked to abnormal serotonin function (reviewed in (Pettinati et al., 2003)). In a meta-analysis of 17 published studies (3,489 alcoholic and 2,325 non-alcoholic subjects) (Feinn et al., 2005), an association was found between frequency of the short (S) allele of the serotonin transporter (5-HTTLPR) and alcohol dependence; this association was stronger among individuals with alcohol dependence complicated by a co-morbid psychiatric condition. However, at this time it is not known whether there are differences between BD-I and BD-II in the association of altered serotonin function with alcohol dependence.

4.4 Early age of onset as a possible moderator for the association of alcohol use disorders and suicide attempts in BD-I

Our observation in BD-I that earlier age of onset was a correlate of suicide attempt in those with alcohol use disorders agrees with prior findings (Dalton et al., 2003; Feinman & Dunner, 1996; Goodwin & Jamison, 1990; Winokur et al., 1995). Individual reports are confirmed by a meta-analysis of 36 studies (including cohort, case-control, and cross-sectional types), which found that among the main risk factors for attempted suicide were alcohol and/or drug abuse and earlier onset of BD (Hawton et al., 2005). One report suggests that early onset of BD-I and alcoholism may share a common genetic etiology (Lin et al., 2006). Early onset of BD also is related to a more severe course of illness (Birmaher et al., 2006) and may be triggered by physical/sexual abuse (Leverich et al., 2003), which in this analysis showed a trend toward a higher rate in BD-I. The present findings show that the effects of earlier onset of BD illness on the association between alcohol use disorder and suicide attempt history were not mainly due to longer duration of illness. Detrimental sequelae of early BD-I onset could include stunted progress in social, academic, or employment spheres, which, speculatively, in context of the increased impulsivity and risk-taking behaviors and/or abnormal mood might combine to influence an adolescent toward injudicious use of alcohol. This hypothesis is consistent with one study of the relationships between BD age of onset and alcohol use disorders that found early onset of BD predicted synchronicity between bipolar symptom changes and drinking. (Fleck et al., 2006) However, it not possible from this dataset to state whether earlier onset of BD triggered onset of SUD or vice-versa.

4.5 Limitations

One limitation of this study is the retrospective design, including the outcome measure of prior suicide attempt, with no information as to chronologic relationship between substance use, mood episode, and suicide attempts. Additionally, as most subjects were in a current Major Depressive Episode, we may have selected against people who spend more time in a hypomanic or manic state, although our bias is consistent with population morbidity patterns of greater time spent in a depressed state, in both BD-I (Judd et al., 2002) and BD-II (Judd et al., 2003). Finally, this is a referred sample, in which the rates of suicide attempters are high; the findings may not generalize to community samples of BD-I and II.

5. Conclusions

Alcohol and other drug use disorders appear to be particularly salient factors for increasing suicide risk in BD-I, along with aggressive/impulsive traits. Future studies in BD-I should target temporal relationships between illness phase, aggressive behavior, substance use and suicide attempts. Successful clinical management of substance use disorders in BD-I may be critical to reduce the risk of suicidal behavior in this population.

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Figure 1. Putative Mediators and Moderators of the Impact of Substance Use Disorders on Suicide Attempt in Bipolar I Disorder

Hypothetical schematic model of relationships between clinical characteristics found to be relevant to history of suicide attempt in Bipolar I Disorder. Factor 1, resulting from a principal component analysis, explains 69% of the variance among the highly correlated variables impulsivity, hostility, and aggressivity.

Table 1
Demographic and Clinical Characteristics of Bipolar I and Bipolar II Patients

Demographic Characteristics	Bipolar I Patients (N=96)				Bipolar II Patients (N=42)				Analysis		
	N	Mean (SD)	Median	Q. Range	N	Mean (SD)	Median	Q. Range	t	df	p
Age (years)	95	37.2 (11.2)			42	37.61 (10.3)			-0.19	135	0.853
Body-mass index	92	27.7 (7.2)			41	26.1 (5.1)			1.57	105.3 ^a	0.120
Education (years)	90	14.9 (2.7)			42	15.1 (2.5)			-0.59	130	0.588
Income level (US\$1000/yr) ^b	84	17.4 (17.5)	14	21	40	25.6(27.7)	17	50		-0.98	0.329
	N		N with characteristic (%)		N		N with characteristic (%)		X ²	df	p
Male sex	96		27 (28.1)		42		16 (38.1)		1.35	1	0.245
White race	96		56 (58.3)		41		33 (80.5)		6.20	1	0.013
Married	94		28 (29.8)		42		14 (33.3)		0.17	1	0.679
Clinical Characteristics	N	Mean (SD)			N	Mean (SD)			t	df	p
Barratt Impulsivity Scale	85	64.3 (19.5)			40	60.2 (18.5)			0.85	123	0.395
Buss-Durkee Hostility Inventory	84	41.9 (13.0)			39	39.9 (14.1)			0.76	121	0.448
Brown-Goodwin Aggression Scale	87	21.6 (6.9)			39	20.5 (6.6)			0.90	124	0.368
Hamilton Depression Scale (17-item)	90	17.4 (6.9)			42	15.5 (8.4)			1.41	130	0.162
Beck Depression Inventory	50	25.4 (11.0)			32	25.8 (13.5)			-0.17	80	0.865
Beck Hopelessness Scale	85	10.8 (5.8)			41	11.8 (5.6)			-0.86	124	0.390
Age at first episode (any type)	89	17.7 (9.1)			41	19.9 (11.3)			-1.15	128	0.251
Reasons for Living Inventory	71	153.1 (50.3)			35	151.1 (40.5)			0.21	104	0.837
Global Assessment Scale	86	46.8(13.4)			39	52.1 (13.5)			-2.02	123	0.045
	N	Mean (SD)	Median	Q. Range	N	Mean (SD)	Median	Q. Range		z	P
No of major depressive episodes ^c	74	9.1 (6.8)	6.0	9	33	7.1 (6.3)	5.0	9		-1.65	0.098
Scale of Suicidal Ideation	74	9.9 (10.2)	5.5	20	36	9.6 (9.80)	8.0	17		-0.09	0.930
	N		N with characteristic (%)		N		N with characteristic (%)		X ²	df	P
Cigarette smoker	90		46 (51.1)		41		17 (41.5)		1.05	1	0.305
Borderline Personality Disorder	82		36 (43.9)		39		13 (33.3)		1.23	1	0.268
History of physical/sexual abuse ^d	88		54 (61.4)		40		18 (45.0)		2.99	1	0.084

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Demographic Characteristics	Bipolar I Patients (N=96)	Bipolar II Patients (N=42)	Analysis
Comorbid anxiety disorder	96	42	18 (42.9) 1.00 0.319

These clinical variables were also tested as modulators of substance use disorders on suicide attempt risk in subjects with Bipolar I.

^aThis comparison did not pass Levene's Test for Equal Variances and so was analyzed under the assumption of non-equal variances, which alters the degrees of freedom (df) term.

^bFor variables with very skewed distributions, the Mann-Whitney test was used;

^cto reduce inaccuracy, the top category includes 20 or more depressive episodes;

^dby self-report. Q, Range = Interquartile Range.

Table 2
Summary of Relationships Between Suicide Attempts, Bipolar Diagnosis, and Substance Use Disorders

	Bipolar I	Bipolar II	χ^2	df	p
<i>No. (%) of Suicide Attempters / Total Subjects:</i>					
	75/96 (78%)	30/42 (71%)	0.72	1	0.396
<i>No. (%) with Substance Use Disorder / Total Subjects:</i>					
+ drug use disorder	42/96 (44%)	17/42 (41%)	0.13	1	0.721
+ alcohol use disorder	47/96 (49%)	22/42 (52%)	0.14	1	0.711
+ both drug & alcohol use disorders	30/96 (31%)	15/42 (36%)	0.27	1	0.607
<i>No. (%) with Substance Use Disorder / Suicide Attempters:</i>					
+ drug use disorder	39/75 (52%)	11/30 (37%)	2.02	1	0.155
+ alcohol use disorder	42/75 (56%)	15/30 (50%)	0.31	1	0.666
+ both drug & alcohol use disorders	29/75 (39%)	9/30 (30%)	0.70	1	0.502
<i>No. (%) of Suicide Attempters / Substance Use Disorder Subjects:</i>					
+ drug use disorder	39/42 (93%)	11/17 (65%)	7.42	1	0.006
- drug use disorder	36/54 (67%)	19/25 (76%)	0.70	1	0.402
+ alcohol use disorder	42/47 (89%)	15/22 (68%)	4.68	1	0.031
- alcohol use disorder	33/49 (67%)	15/20 (75%)	0.39	1	0.531
+ both drug & alcohol use disorders	29/30 (97%)	9/15 (60%)	10.24	1	0.001
- neither drug nor alcohol use	23/37 (62%)	15/20 (75%)	0.96	1	0.389

Significant results are indicated in bold ($p < 0.05$).

Table 3
Effects of Drug or Alcohol Use Disorders and Bipolar Diagnosis on Likelihood of Suicide Attempt

Drug Use	χ^2	df	p	OR	95% CI
Bipolar I vs. II	0.70	1	0.40	0.63	0.22 to 1.86
Drug use disorder	0.69	1	0.43	0.58	0.15 to 2.24
Bipolar I * drug use disorder	6.36	1	0.01	11.23	1.72 to 73.51
Alcohol Use	χ^2	df	p	OR	95% CI
Bipolar I vs. II	0.39	1	0.53	0.69	0.21 to 2.23
Alcohol use disorder	0.24	1	0.63	0.71	0.19 to 2.76
Bipolar I * alcohol use disorder	3.82	1	0.05	5.70	1.00 to 32.65