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Does First Episode Polarity Predict Risk for Suicide Attempt in Bipolar Disorder?

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Abstract

Background— Defining bipolar disorder (BD) subtypes with increased risk of suicidal behavior may help clinical management. We tested the hypothesis that the polarity of a patient's first mood episode would be a marker for BD subtypes with differential risk for suicidality.

Methods— 113 subjects with DSM-IV defined BD were classified based on whether their first reported episode was manic/hypomanic (FM) or depressed (FD). They were compared on demographic and clinical variables. Logistic regression adjusting for potential confounds tested the association between first episode polarity and history of suicide attempt.

Results— Multiple logistic regression analysis showed that FD group membership was associated with eightfold odds of a past suicide attempt, adjusting for years ill and total number of lifetime major depressive episodes.

Limitations— Sample size, retrospective design, recall bias, assessment during a mood episode, and imprecise recall of hypomania.

Conclusions— Polarity of patients' first reported mood episode suggested a depression-prone subtype with a greater probability of past suicide attempt. The FM group had more alcoholism and psychosis, but less likelihood of past suicide attempt. Validation of these putative subtypes requires prospective study.

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*Conflict of Interest

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Keywords

Bipolar Disorder; Suicide; impulsivity; alcohol misuse; hostility

INTRODUCTION

Better understanding of clinical heterogeneity in BD may aid research and improve treatment. Almost 30% of persons with BD make a suicide attempt (Chen et al., 1996). Bipolar patients are most at risk for suicidal behavior during depressive episodes (Goldberg et al., 2002) and dysphoric mania (Rihmer et al., 2002).

Some studies suggest the course of BD is associated with the polarity of the initial episode (Perlis et al., 2005;Perris et al., 1966;Perugi et al., 2000;Roy-Byrne et al., 1985). Quitkin et al. suggested the existence of two subtypes of BD - a manic-prone subtype with a tendency to have more lifetime manic episodes, and a depressive-prone subtype with a higher frequency of depressive episodes (Quitkin et al., 1986). Calabrese found that mood state at study entry predicts polarity at relapse (Calabrese et al., 2004). Perlis et al. found that, in BD-I patients, those whose initial episode was depressive had more lifetime depressive episodes and greater probability of suicide attempt although the latter finding was not significant after adjustment for confounds (Perlis et al., 2005).

In this retrospective study, we attempted to replicate the findings of Quitkin and Perlis in an independent sample, with a focus on suicidal behavior. We hypothesized that a first episode of depressive polarity would be associated with increased likelihood of past suicidal behavior.

METHODS

Subjects

The sample comprised consecutively enrolled inpatients (N=73, 65%) and outpatients (N=40, 35%) diagnosed with BD who sought evaluation and treatment in our research clinic. Axis I and II diagnoses were based on the Structured Clinical Interview for DSM-IV (SCID)(First et al., 1994) and a consensus conference in which all available data were reviewed by experienced research clinicians. Patients were in a mood episode, mostly depressive, at study entry. After complete description of the study, patients signed written informed consent as approved by the Institutional Review Board.

Subjects were grouped based on whether their first lifetime mood episode was manic or hypomanic (FM, N=30 (27%)) or depressed (FD, N=83 (73%)). This was ascertained using the SCID chronology of age of onset of first major depressive, manic, or hypomanic episode. This section does not assess age of onset of first mixed episode. We excluded subjects (N=31) where the age of first depressive and first manic or hypomanic episode was the same since this could be explained either by a mixed episode or sequential episodes in the same year.

Measures

The SCID was used to assess total number of episodes of mania, depression and hypomania prior to baseline assessment. Because subjects were in a mood episode at baseline assessment, we did not analyze state measures. Participants were administered the Brown-Goodwin Aggression Inventory (BGAI)(Brown et al., 1979), the Buss-Durkee Hostility Inventory (BDHI)(Buss et al., 1957), and the Barratt Impulsivity Scale (BIS)(Barratt, 1965).

Suicide attempt history was assessed using the Columbia Suicide History Form (Oquendo et al., 2003) and ideation was assessed with the Scale for Suicidal Ideation (SSI)(Beck et al.,

1979). The Lethality Rating Scale (LRS)(Beck et al., 1975) was used to rate medical damage of suicide attempts. The attempts had a mean lethality score of 3.6 (SD= 2.0, range 0–7) (scored 0 to 8: 0=no medical damage, 4=medical hospitalization required, 8=death). Reasons for living were measured with the Reasons for Living Scale (RFLS)(Linehan et al., 1983). Raters were Masters or PhD-level psychologists. Inter-rater reliability for clinical scales was good to excellent (ICC 0.71 – 0.97)(Mann et al., 1999).

Statistical Methods

The FM and FD groups were compared on quantitative variables using t-tests or Mann-Whitney tests, as appropriate. Categorical variables were analyzed using Chi-square tests. Logistic regression analysis was used to test a clinical model, based on the literature, to investigate the relationship between suicide attempt history and the polarity of the first mood episode. Polarity of initial episode, years ill, number of major depressive episodes (excluding the first episode in the FD group), and the interaction between polarity and lifetime MDEs were included as independent variables. Presence or absence of a lifetime suicide attempt was the dependent variable. To examine potential confounds, we tested exploratory models, adjusting for variables associated with initial episode polarity: BD subtype (I vs. II/NOS), age, reasons for living, impulsivity, hostility, history of alcohol abuse/dependence, number of lifetime manic episodes (excluding first episode in the FM group), interaction between lifetime manic episodes and first episode polarity, number of lifetime psychotic episodes and history of psychotherapy. In each exploratory model, the original model was conserved, adding a single potential confound.

RESULTS

Socio-demographic and Clinical Factors

Seventy-five patients (66.4%) were diagnosed with BD-I at baseline, while 38 (33.4%) were diagnosed with BD-II. The mean age was 38 years (SD=12.6, range 17–73 years), 29% were married, and 57% were female. Seventy-four patients (66%) reported at least one suicide attempt lifetime. Suicide attempters in the sample had made an average of 2.6 attempts (SD=1.9, range 1–11), defined as self-injury with intent to die.

Bonferonni correction for 22 tests would set significance at $p<0.002$. Using this threshold, the FD group reported more years ill, more depressive episodes, and a greater total number of mood episodes (Table 1). There were no other between-group differences. Using a less conservative significance cutoff of $\alpha=0.01$, the FD group was, on average, older at baseline assessment, less likely to be diagnosed Type I BD, less likely to have co-morbid alcohol use disorder, reported fewer reasons for living, and was more likely to report a history of psychotherapy (Table 1). The FD and FM groups did not differ in gender distribution, proportion married, co-morbid Cluster B or drug use disorder, lifetime aggression, impulsivity or hostility, number of manic episodes, or hospitalizations. The groups did not differ in age of first mood episode, first hospitalization, or first psychotropic medication (Table 1).

Suicidal Behavior

The FD group was more likely to have a lifetime history of suicide attempt. FD group attempters had made twice as many suicide attempts as FM group attempters. The groups did not differ in age of first attempt, medical severity of the most lethal past attempt, or reported suicidal intent preceding the most medically serious attempt (Table 2).

Logistic regression analysis

We performed multiple logistic regression analysis of prior suicide attempt status to examine its relationship to first episode polarity. We tested exploratory models adjusting for variables associated with initial episode polarity in bivariate tests. Since suicidal behavior in BD has been associated with depressive symptoms, and since the more years someone is ill, the more time they have to make an attempt, our primary model included the following independent variables: polarity of initial episode, years ill, number of major depressive episodes (excluding the initial episode for the FD group), and the interaction between first episode polarity and number of major depressive episodes.

Results showed that FD group membership was associated with eightfold odds of a lifetime history of suicide attempt, adjusting for years ill and total number of lifetime major depressive episodes (Wald −2.10; OR 8.33; 95% CI 1.85 to 33.33; p=0.005). Years ill, number of lifetime major depressive episodes and its interaction with first episode polarity were not significant predictors.

To the above model, we sequentially added variables associated at $p<0.05$ in bivariate tests with initial episode polarity. The results did not change substantially after sequentially including the following additional covariates: BD-I vs. II/NOS subtype, age, impulsivity, history of alcohol use disorder, history of psychotherapy, number of lifetime psychotic episodes, number of lifetime manic episodes (excluding the first episode in the FM group), and the interaction between lifetime manic episodes and first episode polarity (data not shown).

When reasons for living was added to the model, it was inversely associated with suicide attempt history (Wald 6.28; OR 0.98; 95% CI 0.97 to 1.00; p=0.01). In this model, initial episode polarity was no longer significant (Wald 1.30; OR 3.02; 95% CI 0.45 to 20.22; p=0.25), and no other variable was associated with suicide attempt status (data not shown). However, this model included only 70 cases (out of 100 in the original model) due to missing data.

When we added hostility to the original model, first episode polarity was still significant with a slightly lower odds ratio (Wald 4.30; OR 7.07; 95% CI 1.11 to 44.94; p=0.04). Hostility was also associated with suicide attempt status (Wald 5.70; OR 1.06; 95% CI 1.01 to 1.11; p=0.02). A five-point increase in Buss-Durkee hostility score was associated with a 34% greater odds of a prior suicide attempt (data not shown).

DISCUSSION

The main finding of this study is that in persons with BD, a first reported mood episode of depressive polarity is associated with eightfold greater odds of suicide attempt. This was not explained by years ill, lifetime number of major depressive episodes, or BD-I vs. II/NOS subtype. Hostility was associated with suicide attempt risk, consistent with previous reports from our group (Grunebaum et al., 2006;Oquendo et al., 2000). Reasons for living appeared to be an important protective factor. Our results are consistent with a report from Spain that used a larger sample but did not adjust for years ill and number of major depressive episodes (Daban et al., 2006) and those of Quitkin (Quitkin et al., 1986) and Perlis (Perlis et al., 2005) suggesting a depression-prone bipolar subtype with a higher risk of suicidal behavior.

While the FM group had a large percentage (83%) of subjects with BD-I disorder, the FD group was 53% BD-I. Furthermore, when the bipolar subtype variable was added to the regression model, it did not explain away the effect of initial episode polarity. Therefore, it is unlikely that the results of this study are completely explained by bipolar I vs. II/NOS differences. Studies of suicide attempt frequency across bipolar I vs. II subtypes have been inconclusive

finding lower (Coryell et al., 1987;Vieta et al., 1997), higher (Rihmer et al., 1990;Stallone et al., 1980), and similar (Endicott et al., 1985) rates.

Patients in the FM group, in some ways, had a more severe course of illness with greater alcohol misuse and more psychotic episodes. The FM group was also younger at study entry, which may suggest a more severe course of illness in that our clinic tends to over-sample treatment-resistant cases.

The risk of suicidal behavior may be lower in bipolar patients during manic episodes (Dilsaver et al., 1994), possibly related to manic grandiosity (Grunebaum et al., 2001). This may relate to our finding that the FM group reported more reasons for living. Others have speculated that mania may have adaptive aspects including a protective effect against suicidal behavior mediated by grandiose optimism or less hopelessness (Brody, 2001;Wilson, 1998).

Lithium treatment has been associated with anti-suicidal effects (Baldessarini et al., 2006). The lower rate of suicidal behavior we found in the FM group may be related to this group being diagnosed sooner with bipolar disorder and therefore more quickly receiving a mood stabilizing medication such as lithium. Prospective studies are needed to confirm whether starting mood-stabilizing medication earlier in the course of illness may reduce the risk of suicidal behavior.

The main limitations of this study are relatively small sample size and retrospective design. Our research clinic tends to over-sample suicide attempters, which may have limited our findings in the smaller FM group. Subjects were in a mood episode at study entry, which may have affected data collection and recall bias. Imprecision in patient recall of past hypomanic symptoms, may have influenced results. Our excluding subjects who reported the same age of onset of first depressive and manic or hypomanic episode may have introduced bias. Some of these presumably had a first episode of mixed type while others had sequential episodes in the same year. We did not have data to definitively distinguish these possibilities. It is difficult to gather prospective data on bipolar patients' first mood episodes since large at-risk samples and long follow-up periods are required.

Our results support a limited number of studies suggesting that initial episode polarity may be associated with clinical subtypes of bipolar disorder. We found the FD group incurred a higher risk for suicide attempt above and beyond years ill or number of depressive episodes. These findings may aid sample selection for genetic and other studies. It may be appropriate to monitor bipolar patients whose first reported episode was depressed more closely in relation to risk of suicidality.

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Table 1

Relationship of First Episode Polarity to Clinical and Demographic Variables in 113 Patients with Bipolar Disorder

	First Episode—Manic/Hypomanic N=30		First Episode—Depressive N=83		Chi-square, t-test, Mann- Whitney (Z) or	df	p
	Mean (N)	SD (%)	Mean (N)	SD (%)			
Age	32.2	11.9	40.0	12.3	(−2.89)		0.004
Sex (Female)	(16)	(53%)	(48)	(58%)	0.15	1	0.70
Married	(9)	(30%)	(24)	(29%)	0.02	1	0.89
Reasons for Living scale	183.2	42.8	148.8	44.6	(−2.98)		0.003
Brown Goodwin Aggression Inventory	18.8	5.0	20.1	6.6	(−0.56)		0.58
Barratt Impulsivity Scale	50.3	19.5	60.7	19.2	(−2.06)		0.04
Buss-Durkee Hostility Inventory	31.7	11.3	39.4	13.7	(−2.32)		0.02
Years Ill	8.00	9.2	18.7	12.2	(−4.47)		<0.001
Age of 1st Mood Episode	23.9	8.5	21.2	11.7	(−1.95)		0.05
Age of 1st Psychiatric Hospitalization	26.3	9.8	31.7	12.2	(−1.95)		0.05
Age of 1st Psychotropic Medication	25.2	11.2	28.7	10.7	(−1.43)		0.15
Age of 1st mood stabilizer or neuroleptic	27.7	10.9	33.7	11.5	(−1.90)		0.06
DSM-IV bipolar subtype: Bipolar I	(25)	(83%)	(44)	(53%)	6.13	1	0.01
Cluster B Personality Disorder	(6)	(20%)	(29)	(35%)	0.14	1	0.71
History of Alcohol Abuse/Dependence†	(9)	(30%)	(7)	(8%)	8.26	1	0.01
Hx of Drug Abuse/Dependence †	(5)	(17%)	(10)	(12%)	0.35	1	0.54
Lifetime Major Depressive Episodes	3.4	6.2	8.3	7.0	(−4.66)		<0.001
Lifetime Manic Episodes	4.1	5.2	4.3	6.7	(−2.02)		0.04
Lifetime Psychotic Episodes	1.9	4.0	0.8	3.0	(−3.34)		0.001
Total Number of Episodes (MDE and Mania/ hypomania)	7.6	11.0	12.6	12.0	(−3.04)		0.002
History of Psychotherapy†	(20)	(67%)	(71)	(86%)	10.70	1	0.003
Number of Hospitalizations	3.2	3.7	4.3	8.4	(−0.47)		0.64

Note: Bonferroni correction would set significance at p<0.002

† Fisher's Exact Test

Table 2

Relationship of First Episode Polarity to Suicidality in 113 Patients with Bipolar Disorder

	First Episode—Manic/Hypomanic N=30		First Episode—Depressive N=83		Chi-square, Mann-Whitney (Z)	df	p
	Mean (N)	SD (%)	Mean (N)	SD (%)			
Lifetime History of Suicide Attempt	(14)	(47%)	(61)	(73%)	7.11	1	0.008
Number of Suicide Attempts	0.9	1.1	2.0	2.1	(−2.93)		0.003
Maximum Lethality of Attempts	3.1	2.2	3.8	2.0	(−0.83)		0.41
Suicide Intent Score (for highest lethality suicide attempt)	15.7	5.8	16.0	5.6	(−0.03)		0.98
Age of 1st Suicide Attempt	21.8	10.4	26.8	13.6	(−0.96)		0.34

Note: Bonferroni correction would set significance at p<0.01