Twelve-Month Outcome in Bipolar Patients With and Without Personality Disorders

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Background: We studied the 12-month course of illness after hospitalization for patients with a DSM-III-R diagnosis of bipolar disorder, manic or mixed episode, to identify the impact of a co-occurring personality disorder on measures of outcome.

Method: Fifty-nine patients with bipolar disorder hospitalized for the treatment of a manic or mixed episode were recruited. Diagnostic, symptomatic, and functional evaluations were obtained at the index hospitalization. Personality disorders were assessed using the Structured Clinical Interview for DSM-III-R, personality disorders version (SCID-II). Patients were then reevaluated at 2, 6, and 12 months after discharge to assess syndromic, symptomatic, and functional recovery. Factors associated with outcome were identified using multivariate analyses.

Results: Survival analyses showed that in the 12-month follow-up period, subjects with bipolar disorder and co-occurring personality disorder were significantly less likely to achieve recovery. Logistic regression analyses indicated that both a diagnosis of personality disorder and noncompliance with treatment were significantly associated with lack of syndromic recovery.

Conclusion: Co-occurring personality disorders in patients with bipolar disorder are associated with poor outcome after hospitalization for mania.

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Personality disorders are known to play a role in the outcome of affective disorders, particularly major depression.[1–8] For example, investigators have reported that the presence of a personality disorder in patients with major depression predicts slower treatment response[1] and slower recovery of social function on discharge from the hospital compared with depressed patients without personality disorder.[2] Compared with depressed patients without personality disorder, depressed subjects with personality disorder demonstrate depressive symptoms of greater severity and show less improvement with psychotherapy[3] or tricyclic antidepressants.[4] Depressed patients with and without personality disorder appear to have similar short-term responses to electroconvulsive therapy,[2,5] but one prospective follow-up study suggested that subjects with personality disorder were significantly more symptomatic and 8 times more likely to be rehospitalized.[5] Moreover, poor outcome following a major depressive episode was more common in patients with more than one personality disorder, particularly from multiple DSM-III clusters.[6,7] Thus, in major depression, a co-occurring personality disorder seems to predict chronicity and higher relapse rates.[8]

Despite evidence suggesting that personality disorders occur in up to 60% of bipolar patients,[9–11] the relationship between personality disorders and outcome in bipolar disorder has been little studied. Studies suggest that, in bipolar patients treated with lithium, abnormal personality traits are associated with poor treatment response[12,13] and increased rates of relapse.[14] Coexistence of bipolar and borderline personality disorders is associated with poor response to valproate[15] and poor prognosis.[16] Low levels of social support, maladjustment in social and leisure activities, and poor quality of relationships with extended family have also been associated with poor prognosis in patients diagnosed with bipolar disorder.[17] However, no studies have been published to date that examine the relationship of personality disorder assessed with structured diagnostic instruments to outcome after a manic or mixed episode in bipolar patients.

Previously, we observed a greater prevalence of personality disorder in bipolar patients with prior affective episodes as compared with first-episode patients.[18] This finding suggested an association between personality dis-

orders and poor outcome leading to an overrepresentation of bipolar patients with personality disorder in multiple-episode samples. We prospectively followed these patients for 1 year to further clarify the relationship between bipolar disorder, personality disorder, and outcome. We hypothesized that, consistent with findings in unipolar depression, the subjects with personality disorders would have lower rates of recovery, be less likely to comply with treatment, and be more prone to rehospitalization during the follow-up period.

METHOD

Fifty-nine patients admitted to the University of Cincinnati Hospital psychiatric units were recruited as part of the University of Cincinnati first-episode psychosis and mania projects[19,20] and represent a subset of a larger sample reported previously.[19,20] The demographics, clinical characteristics, and prevalence of personality disorder in this sample have been reported previously.[18] Patients were included for this analysis if they were hospitalized, met DSM-III-R criteria for bipolar disorder (manic or mixed), were between 18 and 65 years old, were able to communicate in English, resided within the Cincinnati metropolitan area, provided written informed consent, and completed the Structured Clinical Interview for DSM-III-R patient (SCID-P)[21] and personality disorders (SCID-II)[22] versions. Patients were excluded if their psychiatric symptoms resulted entirely from acute drug or alcohol intoxication or withdrawal or acute medical illness (e.g., delirium) as determined by medical evaluation and rapid symptom resolution after the medical event. The records of 2 subjects from the original group[18] were unavailable and 1 subject previously included was dropped due to being over 65 years old, yielding 56 subjects available for this analysis.

SCID-P evaluations were performed by psychiatrists with good interrater reliability ($\kappa = 0.94$).[19,20] As part of the SCID-P assessment, the age at onset of bipolar illness was estimated, also with good interrater reliability (intraclass correlation coefficient = 0.90).[19,20] Personality disorder assessments were performed independently by a different psychiatrist (E.D., S.M.S., M.T.S.) using the SCID-II. Interrater reliability was determined from joint ratings of 11 patients as calculated using a weighted kappa statistic, which is recommended for ordinal variables.[23] Interrater reliability was good among raters, ranging from $\kappa = 0.62$ for histrionic personality disorder to $\kappa = 1.0$ for avoidant, obsessive-compulsive, and paranoid personality disorders (for all personality disorders, mean weighted $\kappa = 0.87$). Patients were interviewed with the SCID-II near the time of discharge (a mean of 16 days after the hospital admission), when they had achieved sufficient symptomatic recovery from the affective episode to participate in the interview.[18] Patients were asked to respond to questions on the SCID-II on the basis of how they functioned before becoming ill, or when they felt like their "normal selves." This point was emphasized repeatedly throughout the course of the interview. Within the framework of the SCID-II, the diagnosis of personality disorder is based on DSM-III-R criteria[24] and scored on a 3-point scale (1 = absent, 2 = subthreshold [i.e., some criteria present but diagnostic criteria not met], and 3 = present). For this analysis, a diagnosis of personality disorder was assigned only for a score of 3 or, if 4 or more personality disorders were rated as subthreshold and no other personality disorder was diagnosed, personality disorder not otherwise specified (NOS) was diagnosed,[18] as traits of several personality disorders were present.[24] A diagnosis of personality disorder was also given when criteria were met for the proposed DSM-III-R category of self-defeating personality disorder.[24]

Demographic and treatment variables were obtained from medical records and patient interviews and included age, race (classified as white/nonwhite), sex, educational achievement (in years), medications upon discharge, and employment status rated on a 3-point scale: unemployed, employed unskilled, and employed skilled or student.

Affective symptoms were assessed by research assistants with the Young Mania Rating Scale (YMRS)[25] and the Hamilton Rating Scale for Depression (HAM-D)[26] near the time the SCID-II was completed (with a mean of within 1 day for YMRS and 2 days for HAM-D). Raters had established good interrater reliability with these instruments for YMRS total scores (intraclass correlation coefficient [ICC] = 0.71) and HAM-D total score (ICC = 0.94).[19]

Outcome assessments were scheduled at 2, 6, and 12 months after discharge.[19,20] To assess recovery at each visit, the interviewers concentrated on change points that occurred during the interval, i.e., times when symptoms or function improved or worsened, corresponding to the methodology of the Longitudinal Interval Follow-Up Evaluation (LIFE).[27] Syndromic, symptomatic, and functional recovery and outcome were assessed following the criteria and procedure described in previous reports.[19,20] *Syndromic recovery* was defined as 8 contiguous weeks during which the patient no longer met criteria for a manic, mixed, or depressive syndrome. *Symptomatic recovery* consisted of 8 contiguous weeks during which the patient experienced minimal to no psychiatric symptoms, assessed through YMRS, HAM-D, and scales for assessment of positive and negative symptoms and global functioning.[19,20] *Functional recovery* required a return to premorbid levels of function for at least 8 contiguous weeks. Treatment compliance[28] was defined as (1) *full compliance:* evidence from the patient, clinician, and significant others that medication was taken as prescribed at least 75% of the time; (2) *partial compliance:* evidence that some medications were not taken consistently or that most or all medications were taken intermittently 25% to

Table 1. Demographic and Clinical Characteristics of 56 Patients at Index Hospitalization for Bipolar Disorder, Manic or Mixed[a]

Characteristic	No Personality Disorder (N = 29)	Personality Disorder Present (N = 27)
Age, y, mean (SD)	31 (13)	34 (12)
Female, N (%)	13 (45)	16 (59)
White, N (%)[b]	22 (76)	13 (48)
Education, y, mean (SD)	13 (3)	12 (2)
Employment status, N (%)		
Unemployed	13 (45)	20 (74)
Employed unskilled	6 (21)	3 (11)
Employed skilled or student	10 (34)	4 (15)
Substance use disorder, N (%)[c]	17 (59)	17 (63)
Psychosis, N (%)	26 (90)	22 (81)
Mixed state, N (%)	6 (20)	10 (37)
YMRS score, mean (SD)[d]	16 (11)	17 (9)
HAM-D score, mean (SD)[e]	10 (6)	13 (7)
First episode, N (%)[f]	20 (69)	10 (37)
Previous hospitalizations, mean (SD)[g]	0.7 (1.6)	3.8 (3.8)
Hospitalizations in 12-mo follow-up period, mean (SD)	1.0 (1.4)	1.2 (1.5)
Compliance, N (%)[h]		
Partial or noncompliance	11 (42)	15 (58)
Full compliance	15 (58)	11 (42)

[a]Abbreviations: HAM-D = Hamilton Rating Scale for Depression, YMRS = Young Mania Rating Scale.
[b]$\chi^2 = 4.5$, df = 1, $p < .05$.
[c]Substance use disorder data available on only 26 subjects with personality disorder and 29 subjects without personality disorder.
[d]YMRS data available on only 26 subjects with personality disorder and 28 subjects without personality disorder.
[e]HAM-D data available on only 23 subjects with personality disorder and 23 subjects without personality disorder.
[f]$\chi^2 = 5.7$, df = 1, $p = .01$.
[g]$t = 3.8$, df = 50, $p < .001$.
[h]Compliance data available on only 26 subjects with personality disorder and 26 subjects without personality disorder.

Table 2. Characteristics of Personality Disorders in 56 Bipolar Patients

Personality Disorder	First-Episode Patients	Multiple-Episode Patients
Avoidant	3	5
Dependent	0	2
Obsessive-compulsive	0	2
Passive-aggressive	3	2
Self-defeating	3	2
Paranoid	2	2
Schizotypal	0	2
Schizoid	0	0
Histrionic	0	3
Narcissistic	1	0
Borderline	2	1
Antisocial	1	1
Not otherwise specified	2	2
Total personality disorder diagnoses	17	24
Total patients with personality disorder[a]	10	17

[a]Four patients in each subgroup were diagnosed with more than one personality disorder.

75% of the time or at dosages lower than prescribed; or (3) *total noncompliance:* evidence of medications taken less than 25% of the time or complete discontinuation of all psychotropic medication.

To improve validity of the outcome measures, "best estimate" meetings were held following the completion of the 12-month visits. These meetings included at least 2 psychiatrists or a psychiatrist and a Ph.D.-level psychologist and involved reviewing all assessments from the index hospitalization and outcome assessments, the 12-month diagnostic interview, and any available clinical records. Information from these multiple sources was compared, and a consensus among the research team members was obtained for the occurrence and timing of recovery measures and interval ratings, as described in prior reports.[19,20]

Statistical analyses were performed using the Statistical Analysis System (SAS Institute, Cary, N.C., 1993). We used t tests to assess continuous variables between patients with and without personality disorders, while chi-square analyses evaluated differences in the categorical variables and analyzed associations in the first-episode subgroup between coexistent personality disorder and syndromic, symptomatic, and functional recovery. Kaplan-Meier survival curves were used to estimate the probability of recovery, which was scored as present at the time that it began. The log-rank test determined differences between groups. This analysis was also performed separately for syndromic, symptomatic, and functional recovery. Logistic regression analyses were performed to determine whether personality disorders were associated with syndromic, symptomatic, and functional recovery, controlling for the effects of first episode versus multiple episodes, race, sex, socioeconomic status, age, and compliance. All demographic variables included in these analyses had previously been associated with outcome.[18–20]

RESULTS

Characteristics of the Sample

Table 1 lists the demographic and clinical characteristics of this sample. Thirty patients were in their first episode of mania; 26 had experienced previous episodes. Twenty-seven subjects (48%) were diagnosed with a coexistent personality disorder, and 8 (30%) of those were diagnosed with more than 1 personality disorder (Table 2). Subjects with personality disorders had more prior hospitalizations ($t = 3.8$, df = 50, $p < .001$) and were also less likely to be white ($\chi^2 = 4.5$, df = 1, $p < .05$) or to be experiencing their first manic episode ($\chi^2 = 5.7$, df = 1, $p = .01$). No significant differences were found between the patient groups in sex, education or employment status, mixed state, presence of substance use disorders or psychosis, and mean YMRS and HAM-D total scores (see Table 1). The medications prescribed at discharge from the index hospitalization are described in Table 3. Data from 52 patients (93%) who attended at least one follow-up visit were used for survival analyses. The data from 42

Table 3. Discharge Medications of 56 Subjects With and Without Personality Disorder

Medication	No Personality Disorder (N = 29)	Personality Disorder Present (N = 27)
Mood stabilizer	9	8
Antipsychotic	2	0
Antidepressant	2	0
Mood stabilizer and antipsychotic	0	1
Mood stabilizer and antidepressant	16	15
Antipsychotic and antidepressant	0	0
Combined treatment	0	1
No medications	0	2

patients (75%) who completed the entire 12-month protocol were used for logistic regression analyses.

Syndromic Recovery

Analysis of the survival curves revealed a significant difference between the groups with and without co-occurring personality disorder. The presence of a personality disorder was associated with lack of syndromic recovery (log rank $\chi^2 = 8.0$, df = 1, $p < .005$; Figure 1).

Logistic regression revealed that the presence of a personality disorder ($\chi^2 = 3.8$, df = 1, p = .05, odds ratio [OR] = 5.9, 95% confidence interval [CI] = 1.0 to 35.8) and noncompliance with treatment ($\chi^2 = 4.8$, df = 1, p = .02, OR = 0.14, 95% CI = 0.03 to 0.8) were associated with lack of syndromic recovery. The effects of first- versus multiple-episode status, race, sex, employment status, and age were all nonsignificant. Specifically, 18 (69%) of 26 patients without personality disorder recovered, compared with 9 (35%) of 26 with personality disorder.

Symptomatic Recovery

Ten subjects (38%) without personality disorder achieved symptomatic recovery, compared with only 3 (12%) with personality disorder. Again, analysis of the survival curves revealed a significant difference between the 2 groups (log rank $\chi^2 = 5.4$, df = 1, $p < .05$). Logistic regression revealed no variables associated with symptomatic recovery.

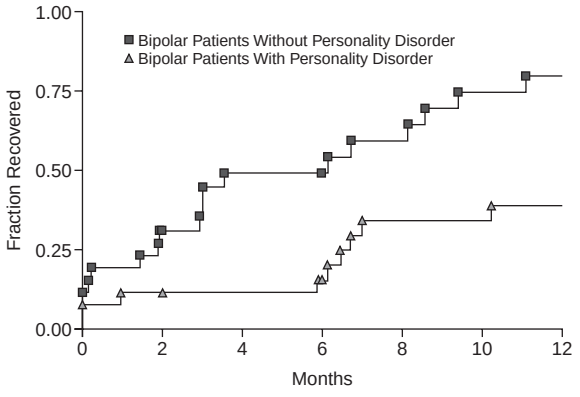
Functional Recovery

Only 8 subjects (31%) without personality disorder and 3 subjects (10%) with personality disorder achieved functional recovery, a significant difference between the 2 groups (log rank $\chi^2 = 6.6$, df = 1, p = .01). Again, logistic regression revealed no variables associated with functional recovery. (Curves for symptomatic and functional recovery omitted for space considerations.)

First-Episode Subgroup

Because of the small group size, only chi-square analyses were performed on this subgroup. There was an association of personality disorder with syndromic recovery ($\chi^2 = 3.6$, df = 1, p = .05), but not with symptomatic or functional recovery.

Figure 1. Survival Analysis of the Fraction of Manic or Mixed Patients With and Without Personality Disorder Achieving Syndromic Recovery Over 1 Year



DISCUSSION

To our knowledge, this is the first report prospectively evaluating associations between DSM-III-R personality disorders and outcome in bipolar patients. Previously, we suggested that personality disorder in bipolar disorder would be associated with poor outcome, thus contributing to the overrepresentation of subjects with personality disorder in our multiple-episode sample as compared with first-episode patients.[18] This prospective study expands on those findings by demonstrating an association of personality disorder with a lower rate of syndromic recovery over the year after an index hospitalization for mania or mixed state. It also shows an association between syndromic recovery and compliance. However, our hypothesis of increased rates of rehospitalization for patients with co-occurring personality disorder was not confirmed in this study.

How personality disorders and affective illness interact to lead to poor outcome is unclear. As suggested by our findings, compliance may be a mediating factor, given its association with syndromic recovery.[20] Thus, lack of adherence to prescribed treatment programs would lead to poor outcome.

Co-occurring personality disorder may also be the hallmark of a more severe or persistent form of affective disorder. For example, Akiskal et al.[29] reported that, in subjects with a history of major depression, the simultaneous presence of DSM-III-R personality disorders from both clusters B and C is associated with subsequent hypomanic episodes. In this view, abnormal personality appears to be another dimension of the affective illness with important prognostic significance. The finding of an association between personality disorder and syndromic re-

covery in the first-episode group as shown by the chi-square analysis lends some support to this view.

An alternative explanation, consistent with the higher rates of personality disorder in the multiple-episode group, is that symptoms of personality disorder could emerge as sequelae of affective illness.[18,30] In this scenario, repeated episodes of affective dysregulation would predispose the patient to the development of maladaptive characterological traits that would in turn become part of the enduring psychosocial sequelae, at times associated with recurrent affective illness.[31]

It is also possible that personality disorder interviews may simply be sensitive to attenuated symptoms of manic-depressive illness. In this view, rather than indicating the presence of a co-occurring personality disorder, the pathologic findings in the personality domain would be understood as an artifact of the ongoing affective illness rather than true Axis II pathology. This is unlikely, though, given the similar mean HAM-D and YMRS scores in each group.

Several important limitations to our study require consideration when interpreting these results. First, this is a sample of severely ill, hospitalized manic patients. It is unclear how representative this sample may be of the larger universe of bipolar patients, and these results may not be generalizable to patients who are less ill or less depressed or to those in outpatient settings. Second, the diagnosis of personality disorders in patients recovering from a major affective episode is fraught with difficulties since some personality traits, but not all, appear to vary in the presence of affective symptoms.[11,32] Upon interview, these subjects were still experiencing affective symptoms that could distort their view of themselves. A reassessment of personality characteristics after full recovery might have increased the validity of our findings. However, the YMRS and HAM-D total scores were not associated with a diagnosis of personality disorder, suggesting that the 2 are not strongly linked in this sample. Third, patients tend to deny socially embarrassing behaviors,[33] so the lack of informant reports limits the accuracy of the diagnosis of personality disorder. However, it should also be noted that concordance between informant and patient reports is often low,[32] thus complicating the diagnosis of personality disorder. Fourth, because of lack of statistical power, we are unable to determine if any given personality disorder cluster would be predictive of outcome. Finally, because of the characteristics of the clinical interviews performed, it was not possible for the raters to be entirely blinded to the patients' psychiatric history. This lack of blindedness could have biased the interviewers to diagnose more personality disorders in patients with multiple episodes of affective illness and to select for a more chronic and impaired population, but the problem should have been minimized by using multiple and separate SCID-I and SCID-II raters with good interrater reliability.

Despite these limitations, the diagnosis of personality disorder in this study identified a subgroup of bipolar patients significantly less likely to recover from an index manic episode. Additional prospective studies, particularly in young, first-episode subjects, are needed to further elucidate the relationship of personality disorders to hospitalization and outcome in bipolar patients and the impact of recurrent affective illness on personality.

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