Bipolar Disorder and Comorbid Personality Psychopathology: A Review of the Literature

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Objective: To examine the prevalence of personality disorder comorbidity in bipolar disorder and examine the effects of this comorbidity on bipolar disorder patients.

Data Sources: All the studies reviewed were found through an online literature search through the Web site PubMed. The studies were published between 1980 and 2006. The following keywords were used to search articles: *bipolar*, *mania*, *mood*, *personality*, *Axis II*, *borderline*, and *lithium*. Only articles in English were included in this literature review.

Study Selection: A total of 32 studies that reported data on the prevalence and effect of comorbid personality disorders or abnormal personality traits in bipolar disorder patients were reviewed.

Data Extraction: The data abstracted from the prevalence studies included sample size, mood state of the study population, research instruments used to determine personality psychopathology, prevalence rates of personality disorders, and abnormalities. Other data collected included response to medications and course of illness.

Data Synthesis: The prevalence studies were categorized into outpatient and inpatient studies to facilitate data analysis. The prevalence studies were also analyzed according to the research instrument used to measure personality pathology. Studies that used non-DSM personality measures were analyzed separately.

Conclusions: Bipolar disorder patients have significantly higher prevalence of personality disorder than the general population. Several studies reviewed indicate a higher prevalence of Axis II disorders in bipolar patients with unstable mood. However, this finding was not confirmed in comparison of inpatient and outpatient comorbidity rates. Bipolar patients with personality psychopathology have poorer response to medications and a more virulent course of illness.

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In the past 30 years, an increasing number of studies have investigated the relationship between bipolar disorder and personality disorders. Numerous clinical studies have consistently shown a sizable comorbidity of personality disorders in bipolar disorder patients. Fewer studies have examined the impact of comorbid personality disorders on the course of illness and on the treatment response to medications. A review of these topics may provide insight into the impact of Axis II psychopathology on clinical and functional outcomes in bipolar disorder as well as other psychiatric disorders. Conversely, this literature may also provide insights on the effects of mood instability on personality psychopathology. These insights may provide an indication of the extent to which personality disorders can be treated by medications used in bipolar disorders. Systematically analyzed, these studies may give a greater understanding of the relationship of mood and personality in general.

Methodological challenges complicate the study of the comorbidity of bipolar disorder and personality disorders. A primary challenge is distinguishing the symptoms of mood states from those of personality disorders. This distinction can be particularly difficult in bipolar patients who are not clinically stable. Mood symptoms can potentially influence patients' perception and report of personality traits. This challenge relates to unresolved theoretical and diagnostic dilemmas within the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) system. Within the DSM system, mood disorders are diagnosed by the concurrent presence of mood-related symptoms. In contrast, a personality disorder is defined as "an enduring

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pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture and is manifested in cognition, affectivity, interpersonal functioning, or impulse control."[1(p630)] This enduring pattern leads to clinically significant distress or impairment in social or occupational functioning. This apparent distinction does not always prove to be clinically useful. The impulsivity, aggression, and reckless disregard for safety seen in antisocial personality disorder can also be present in mixed mania. The grandiose and entitled attitude and behavior in narcissistic personality disorder can also be symptoms of hypomania. The distinction between bipolar disorders and borderline personality disorder can be particularly difficult to discern, as described in an excellent case study by Bolton and Gunderson.[2] Self-harm behavior, mood instability, unstable relationships, and intermittent paranoia can be present in both disorders. Although studies have shown differences in longitudinal course, medication response, family psychiatric history, and phenomenology in these 2 disorders, research instruments may not account for these factors.[3]

Quantification of personality psychopathology is another methodological challenge in the study of personality disorders. Multiple theoretical models and scales have been developed to measure personality traits. Many studies have used DSM-based categorical assessments for personality disorder, and others have used dimensional and non–DSM-based measurements of personality traits. In this review, the studies that used DSM-based instruments were examined separately from studies that used different theoretical models of diagnosis and personality. Interrater reliability was poor in the early studies with DSM-based diagnostic instruments. Subsequent studies used structured interviews, intensive training of raters, and counterbalancing of raters to elevate the reliability of personality disorder diagnosis to acceptable levels.[4] Nonetheless, studies have consistently found lower interrater reliability for categorical diagnosis compared to dimensional personality measures in these instruments.[5–7]

All of the studies reviewed for this article sampled from clinical settings. The prevalence rates of these studies differ from those of epidemiologic studies on bipolar disorder and personality disorder. Epidemiologic studies indicate the prevalence of bipolar I to be 1.6% and the combined prevalence of bipolar I and II to be 2.8%–3.7%.[8–10] A number of studies have estimated the prevalence of personality disorders to be 5.9% to 17.9% of the population.[11–15] In contrast, the comorbidity rate of personality disorders in the bipolar studies reviewed ranged from 12% to 89% (Tables 1 and 2).[16–31,32,42–45] No studies were found that investigated this comorbidity in a nonclinical population.

This article will review 32 studies that measure the prevalence of personality disorders and abnormal personality traits in bipolar disorders. This article will then review the studies on the impact of personality disorders on the illness course and medication efficacy for bipolar disorder. All the studies reviewed were found through an online literature search through the Web site PubMed. The studies were published between 1980 and 2006 (mostly after 1990). The following keywords were used to search articles: *bipolar*, *mania*, *mood*, *personality*, *Axis II*, *borderline*, and *lithium*. Only articles published in or translated into English were included in this literature review. All the articles were then obtained through the University of California, Los Angeles health sciences library or a publisher's Web site.

THE PREVALENCE OF PERSONALITY DISORDERS IN OUTPATIENT BIPOLAR POPULATIONS

The studies on the comorbidity of bipolar disorder and personality disorders can be usefully divided into outpatient and inpatient studies. There are enough studies in each group so that useful comparisons can potentially be made within each group and between the 2 groups. Because bipolar outpatients are generally less symptomatic than hospitalized bipolar patients, trait versus state questions are potentially less problematic in an outpatient setting. In these studies, self-report questionnaires and structured interviews have all been used to assess personality psychopathology. Most of the studies on the prevalence of Axis II disorders in bipolar disorder use the following DSM-based structured interviews: Personality Disorder Examination (PDE), Structured Interview for DSM-III Personality Disorders (SIDP), and the Structured Clinical Interview for DSM-III-R and DSM-IV Personality Disorders (SCID-II). The outpatient comorbidity studies are summarized in Table 1.

Of all the outpatient comorbidity studies, 3 studies have particular significance.[20,24,25] These studies not only assess the prevalence of personality disorders in bipolar disorder, but also explore important issues in the methodology of assessing the prevalence of personality disorders. They highlight the shortcomings of the majority of studies on this topic. Kay et al.[25] examined 61 euthymic bipolar I patients for personality disorders. The authors used the SCID-II (DSM-III-R version) and the Personality Diagnostic Questionnaire (PDQ) to assess Axis II pathology. This study is unique in comparing the results of self-ratings and structured interviews. Their results indicated that the self-report PDQ consistently overdiagnosed personality disorders, finding 62% of the bipolar subjects with an Axis II disorder. Based on the SCID-II, 38% of patients had a personality disorder. The authors further found that the subjects with comorbid alcoholism had a higher rate of personality disorder than those without comorbid alcoholism (52% vs. 24%, respectively). Cluster A personality disorders (schizoid, schizotypal, paranoid) were more common in alcoholic bipolar patients.

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Table 1. Axis II Comorbidity in Bipolar Outpatient Studies

Study	N	Axis II Diagnostic Instrument[a]	Patient Population	Prevalence of Any Personality Disorder, %
Kutcher et al[16]	20	PDE	Euthymic adolescents (19 outpatients, 1 inpatient)[b]	35.0
O'Connell et al[17]	50	PDQ-R	Outpatients taking therapeutic doses of lithium	58.0
Alnaes and Torgensen[18]	19	SIDP	Patients referred to a psychiatry clinic	84.0[c]
Gasperini et al[19]	54	SIDP	Euthymic patients taking lithium maintenance	63.0
Peselow et al[20]	47	SIDP	Euthymic patients	44.7[d]
Flick et al[21]	54	SCID-II	Bipolar and cyclothymic patients	70.3[c]
Carpenter et al[22]	23	PDE	Married euthymic patients	22.0
Barbato and Hafner[23]	42	PDE	Euthymic bipolar I patients in remission	45.0
Ucok et al[24]	90	SCID-II	Euthymic bipolar patients	47.7
Kay et al[25]	61	SCID-II; PDQ	Euthymic bipolar I patients	38.0; 62.0
Vieta et al[26]	40	SCID-II	Euthymic bipolar II patients in remission	32.5
Benazzi[27]	50	SCID-II	Bipolar II patients with depressed mood	12.0
Colom et al[28]	200	SCID-II	Euthymic bipolar patients in remission	26.0
George et al[29]	52	PDE	Bipolar patients in relative remission	28.8
Brieger et al[30]	60	SCID-II	Bipolar patients recently discharged from psychiatric hospital	38.0
Loftus and Jaeger[31]	51	SCID-II	Bipolar I patients (47 outpatients, 4 inpatients)	45.0

[a]The PDE, SIDP, and SCID-II are structured interviews; the PDQ-R is a self-report questionnaire.
[b]Adolescent subjects had an average age of 17.5 years.
[c]No control for mood state of subjects at time of testing.
[d]55.3% when informant reports were used.
Abbreviations: PDE = Personality Disorder Examination, PDQ-R = Personality Diagnostic Questionnaire-Revised, SCID-II = Structured Clinical Interview for DSM-III-R Personality Disorders, SIDP = Structured Interview for DSM-III Personality Disorders.

Ucok et al.[24] compared 90 euthymic bipolar patients with 58 controls (no history of mental illness). Using the SCID-II (DSM-III-R version), they found 47.7% of the bipolar patients and 15.5% of control patients with at least 1 personality disorder. Ucok and colleagues' study[24] was unique among the outpatient studies in having a control group. Peselow et al.[20] followed 47 bipolar patients from a hypomanic episode until recovery to a euthymic mood. In this study, the SIDP was administered to the patient and an informant during the hypomanic episode and after recovery from the episode. The informants were relatives or friends of the patients who were chosen by the patients to give information about the patient. The results of this study showed that during the hypomanic episode, informants reported a slightly higher rate of Axis II psychopathology (57.4%) compared to the patients (53.2%). Both patients and informants reported a reduction in all maladaptive personality traits except schizoid and avoidant traits after recovery from the hypomanic episode. However, informants still reported a higher rate of Axis II psychopathology than patients in euthymic mood (55.3% vs. 44.7%, respectively). The informant data from this study challenge the results of studies that only collect data from subjects. The importance of an informant group to give observations on the subjects' behavior has been identified in other personality disorder studies.[32–34]

The effect of mood state on personality disorder measures is evidenced in 3 studies that use the SCID-II.[21,28,30] Flick et al.[21] administered the SCID-II (DSM-III-R version) to 54 bipolar and cyclothymic subjects. Mood state was not controlled at the time of SCID-II interview. This study reported a high rate of comorbidity (70.3%) of the subjects having at least 1 personality disorder. Brieger and colleagues[30] found a lower comorbidity rate (38%) in 60 bipolar patients recently discharged from a psychiatric hospital who were "largely in remission." Colom et al.[28] conducted the largest outpatient comorbidity study, with 200 bipolar patients in remission. This study collected data from the subjects and at least 1 close relative or partner and found a comorbidity rate of 26%.

Alnaes and Torgensen[18] administered the SIDP to 19 bipolar patients referred to a psychiatry clinic. Sixteen of the 19 subjects (84%) were determined to have a personality disorder. Dependent personality disorder was the most common personality disorder (47%) found. This study reported the highest rate of Axis II comorbidity in an outpatient sample. The high rate of Axis II comorbidity may be due to the small sample size and no control of the mood state at the time of SIDP interview. However, Gasperini and colleagues,[19] using the SIDP to study bipolar subjects (N = 54) with euthymic mood on lithium maintenance, also found a relatively high comorbidity rate (63%). The most common personality disorder found in this study was histrionic personality disorder.

Several studies used the PDE.[16,22,23,29] Carpenter et al.[22] assessed 23 married euthymic bipolar patients. Twenty-two percent of this sample were found to have a personality disorder. Barbato and Hafner[23] studied 42 bipolar I disorder patients in remission and found a 45% prevalence of personality disorders. George and colleagues[29] examined 52 bipolar subjects in "relative remission," of which 28.8% had at least 1 personality disorder.

Only 2 studies[26,27] were found on the prevalence of personality disorders in bipolar disorder type II. Vieta et al.[26]

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Table 2. Axis II Comorbidity in Bipolar Inpatient Studies

Study	N	Axis II Diagnostic Method[a]	Inpatient Population	Prevalence of Any Axis II Disorder, %
Charney et al[42]	30	Retrospective review of hospital charts	Patients in depressive episode	23.0
Pica et al[32]	26	SIDP	16 bipolar and 10 schizoaffective, bipolar type, patients	42.0[b]
Turley et al[43]	21	SIDP; MCMI-II	Recent onset bipolar patients	58.0; 89.0
Dunayevich et al[44]	59	SCID-II	Patients in manic or mixed episode	48.0
Rossi et al[45]	71	SCID-II	Patients in depressive episode	41.9

[a]The SIDP and SCID-II are structured interviews; the MCMI-II is a self-report questionnaire.
[b]62.0% when informant reports were used.
Abbreviations: MCMI-II = Million Clinical Multiaxial Inventory, SCID-II = Structured Clinical Interview for DSM-III-R Personality Disorders, SIDP = Structured Interview for DSM-III Personality Disorders.

studied 40 bipolar II patients in remission using SCID-II (DSM-III-R version). They found 32.5% had at least 1 personality disorder, with borderline personality disorder as the most common personality comorbidity in this sample. Benazzi[27] studied 50 bipolar II patients who presented to a private practice clinic for depression. He found that 12% of these patients met the diagnostic criteria for borderline personality disorder using the SCID-II (DSM-IV version). Calabrese et al.[35] studied and reported on 101 rapid cycling bipolar subjects. This study found a 27% comorbidity with borderline personality disorder alone. (The method of diagnosing borderline personality disorder was not clarified in the study.)

Several comorbidity studies have reported on heterogeneous bipolar populations. In the largest of these studies, Garno et al.[36] studied 100 bipolar (type I and II) patients, consisting of 95 outpatients and 5 inpatients. This study found a 30% comorbidity rate with a cluster B personality disorder using the SCID-II (DSM-IV version). Loftus and Jaeger[31] studied 51 bipolar I patients (47 outpatients, 4 inpatients) and found a 45% comorbidity with at least 1 Axis II disorder using the SCID-II (DSM-IV version). In the only comorbidity study of a solely adolescent bipolar population, Kutcher et al.[16] assessed a group of 20 euthymic subjects (19 outpatients and 1 inpatient). Thirty-five percent of this group were found to have a personality disorder.

Of the outpatient prevalence studies, only O'Connell and colleagues[17] used a self-report questionnaire, the PDQ-Revised (PDQ-R), exclusively to assess Axis II pathology. In this study, the PDQ-R was given to 50 bipolar outpatients on therapeutic doses of lithium. Twenty-nine of the subjects (58%) met criteria for 1 or more personality disorders with the majority of the Axis II diagnoses from cluster B. This comorbidity rate is higher than the average of comorbidity rates (37.7%) in the studies using structured interviews and euthymic populations.[19,20,22–26,28] This finding is consistent with the results of Kay and colleagues' study[25] and other studies that have found self-report instruments consistently diagnosing personality disorders at a higher rate compared to structured interview instruments.[37–41]

THE PREVALENCE OF PERSONALITY DISORDERS IN INPATIENT BIPOLAR POPULATIONS

A fewer number of studies have also been done to assess the prevalence of personality disorders in hospitalized bipolar patients. Before examining the inpatient studies, the authors of this review hypothesized that hospitalized bipolar patients would show a higher prevalence of personality disorders. A review of the outpatient studies had indicated that stability of mood affected the report of personality disorder symptoms. However, the average comorbidity rate of the 5 inpatient studies (weighted for sample size) was 42.5%. This finding was similar to average comorbidity rate of the outpatient studies (40.2%). Other results of the inpatient studies are consistent with the results of the outpatient studies. The inpatient prevalence studies are summarized in Table 2.

Four of the inpatient studies were done using structured interview instruments. Dunayevich et al.[44] studied 59 bipolar patients hospitalized for mania or a mixed episode. The subjects were assessed for personality disorder by the SCID-II (DSM-III-R version) near time of discharge. Forty-eight percent of the subjects were found to have a comorbid personality disorder, and 13.6% of the subjects had more than 1 personality disorder. In this study, 65% of the patients with multiple manic episodes had a personality disorder compared to only 33% of the patients hospitalized for their first manic episode.[44] This unique finding is further indication that mood instability may affect the severity of personality disorders. Rossi and colleagues[45] studied 71 bipolar patients hospitalized for depression. The SCID-II (DSM-III-R version) was administered when the patients' depressive symptoms were resolving (Hamilton Rating Scale for Depression score < 11). This study found that 41.9% of the patients had at least 1 personality disorder. Obsessive-compulsive personality disorder was found to be the most common personality disorder (32.4%), followed by borderline personality disorder (29.6%), and avoidant personality disorder (19.7%).[45]

Turley et al.[43] studied 21 inpatients with recent onset bipolar disorder using the SIDP and the Million Clinical

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Multiaxial Inventory (MCMI-II). The MCMI-II is a self-report questionnaire developed from a theory driven model distinct from the descriptive DSM system. It diagnoses the 11 DSM-III personality disorders but includes self-defeating and aggressive personality disorders. The SIDP found that 58% of the sample had at least 1 personality disorder. The MCMI-II found that 89% of the sample had at least 1 personality disorder. The results of Turley and colleagues' study[43] were consistent with those of Kay et al.[25] in finding that a self-report instrument showed more personality psychopathology compared to a structured interview. Pica et al.[32] used the SIDP to examine 26 hospitalized bipolar patients (10 of whom had schizoaffective disorder, bipolar type). Subjects and their informants were interviewed for this study. From the data obtained from subjects, 42% of the subjects were found to have personality disorders. Data obtained from informants indicated that 62% of the subjects had at least 1 personality disorder. The informant results are consistent with those of Peselow and colleagues' outpatient study,[20] showing informants reporting a greater severity of personality disorder symptoms than study subjects themselves. Histrionic personality disorder was found to be the most common personality disorder in this study.[32]

Two prevalence studies[42,46] used a retrospective chart review method. Both studies reported relatively low rates of Axis II comorbidity in bipolar populations. Charney et al.[42] retrospectively reviewed the hospital charts of 30 bipolar patients hospitalized for a depressive episode. Twenty-three percent of the patients were assessed to have a personality disorder by DSM-III criteria. The only study that did not separate inpatient and outpatient bipolar populations reviewed the psychiatric charts of 171 bipolar patients who had received either inpatient or outpatient psychiatric care at a university hospital.[46] Using DSM-III criteria, 15 of the bipolar subjects (9%) were assessed to have at least 1 personality disorder.

THE PREVALENCE AND IMPACT OF MALADAPTIVE PERSONALITY TRAITS IN BIPOLAR PATIENTS

A number of studies using non-DSM measures of personality have also been done to understand the interaction of mood and personality in bipolar disorder. Consistent with studies that use DSM-based diagnostic measures, these studies indicate that bipolar patients have higher rates of abnormal personality traits compared to normative groups. Several of these studies also suggest that maladaptive personality traits contribute to a poorer prognosis. These findings are also consistent with those of studies that use DSM-based measures.

Solomon et al.[47] compared the personality traits of subjects with bipolar I disorder in remission to the personality traits of subjects with no history of any mental illness. A total of 30 euthymic bipolar I subjects were compared to 974 never-ill subjects on 17 self-rated personality scales selected for their relevance to mood disorders. This study found that the subjects with bipolar I disorder in remission had more aberrant scores on 6 of the 17 personality measures: emotional stability, objectivity, neuroticism, ego resiliency, ego control, and hysterical factor.[47]

Lozano and Johnson[48] also conducted a study to identify personality traits that predicted the course of manic and depressive symptoms experienced by bipolar patients. The Neuroticism, Extraversion, Openness 5-Factor Inventory was administered to 39 participants with bipolar I disorder in remission. This instrument measured 5 dimensions of personality: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. The results of this study showed that bipolar individuals, compared to a normative sample, scored significantly higher on the neuroticism and openness to experience domains, and significantly lower on the agreeableness domains. This study further showed that participants with high neuroticism appeared more susceptible to increases in depressive symptoms, consistent with previous research on unipolar depression. Participants with high achievement striving were more likely to experience increases in manic symptoms.[48]

Strakowski et al.[49] conducted a study using the Tridimensional Personality Questionnaire (TPQ), which divided personality into 3 temperamental dimensions: novelty seeking, harm avoidance, and reward dependence. In this study, 27 hospitalized patients with first-episode mania were administered the TPQ near the time of discharge to see if personality factors predicted syndromal and functional outcome at discharge and 6 months after discharge. Seventeen patients were in syndromal remission at discharge, and all 27 patients were in syndromal remission 6 months after discharge. There was no correlation between time to syndromal recovery and any TPQ item. Six patients did not achieve functional recovery after 6 months. In those patients who did not functionally recover, the ratings for novelty seeking were significantly higher than in those who achieved functional recover. The most significant differences were in the novelty seeking subdimensions of impulsiveness and disorderliness.[49] Young et al.[50] used the TPQ to compare the personality dimensions of 45 euthymic bipolar patients to 100 nonpatient control subjects. The bipolar group had significantly higher scores on novelty seeking and harm avoidance compared to the nonpatient group.

Turley et al.[43] tested 19 subjects with DSM-III-R diagnoses of bipolar disorder or schizoaffective disorder, bipolar type, with the MCMI-II, which is an instrument that measures personality along 3 underlying dimensions: "self-other" orientation, "active-passive" presentation, and "pleasure-pain" motivation. Narcissistic and antisocial personality disorders had the highest prevalence rates (both 47%), followed by histrionic and passive-

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aggressive disorders (both 37%). The predominant area of personality disturbance was located in difficulties on the "self-other" dimension, specifically, in balancing self-preoccupation and social responsibility.[43]

Heerlein and colleagues[51] conducted a study with 6 bipolar subjects to identify specific personality traits that may influence the clinical course of bipolar disorder. The Munich Personality Test, a 51-item self-report questionnaire, was completed by the subjects and their family informants to measure the following personality dimensions: extroversion, neuroticism, frustration tolerance, rigidity, esoteric tendencies, and isolation tendencies. Clinical outcome was defined by the frequency and severity of relapses, the quality of remission, and the chronicity of symptoms. Heerlein et al.[51] found that self- and family-reported neuroticism and self-reported rigidity have significant correlation to a poor prognostic treatment outcome.

Atre-Vaidya and Hussain[52] reported a study that compared 13 bipolar subjects with 10 subjects with borderline personality disorder using the Temperament and Character Inventory (TCI). The TCI measures 7 dimensions of temperament and character: novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, and self-transcendence. When compared to normative data, the borderline subjects had abnormal scores on the dimensions of harm avoidance, self-directedness, and cooperativeness. The bipolar patients did not show any deviations from normative data.[52] Although limited in sample size, this study is unique in showing bipolar patients having no personality deviations compared to normative data.

THE IMPACT OF PERSONALITY DISORDERS ON THE ILLNESS COURSE OF BIPOLAR DISORDER

A small number of studies have explored the effects of comorbid personality disorders on the course of bipolar disorder. Most of these studies are also limited in having relatively small sample sizes. Using retrospective and prospective designs, all these studies indicate a more virulent illness course for bipolar patients with comorbid Axis II psychopathology. Most of the studies measure clinical outcomes; fewer studies measure functional outcome. Several of these studies indicate an increased lifetime suicidal risk for bipolar patients with cluster B personality disorders. It is difficult to draw other conclusions from comparing these studies, as they use different outcome measures.

In the largest retrospective study, Leverich et al.[53] analyzed data from 648 bipolar subjects from multiple sites and studies. The self-rated PDQ-4+ was used to assess Axis II comorbidity. This study found an increased rate of suicide attempts in bipolar patients with Axis II diagnoses. Patients with cluster B disorder had the strongest association with suicide attempts.[53] The Systematic Treatment Enhancement Program for Bipolar Disorder study of 500 bipolar subjects[54] found that subjects with Axis II comorbidity had more psychosocial service utilization than those without. Garno et al.[36] studied comorbid cluster B personality disorders in a group of 100 bipolar (type I and II) patients. In this study as well, patients with comorbid cluster B disorders were found to have more lifetime suicide attempts.[36] Gaviria et al.[55] conducted a chart review study comparing 75 bipolar patients without psychiatric comorbidity with 13 bipolar patients with comorbid borderline personality disorder. All subjects were followed in the same clinic and maintained on a therapeutic level of lithium (0.8–1.5 mEq/L). This study found that subjects with borderline personality disorder had more psychotic symptoms during their mood episodes than the non-borderline group. The borderline group also reported a higher frequency of childhood and adolescent psychopathology and an earlier age at onset of their first mood episode (21.5 years vs. 32.9 years).[55]

In Kay and colleagues' retrospective study of 52 euthymic male bipolar subjects,[56] the authors also found poorer clinical and functional outcome in the subjects with comorbid Axis II psychopathology. This study found that Axis II comorbidity was associated with a higher prevalence of substance abuse, more psychiatric medications prescribed, and more unemployment. George et al.[29] examined 52 bipolar patients in relative remission. Patients with personality disorders were found to have more severe manic symptoms. This study also showed cluster C (fearful, avoidant) dimensional scores were positively correlated with depression scores. However, this study did not find any difference in the number of prior episodes or hospitalizations between the subjects with and without personality disorders.[29] Vieta et al.[26] studied 40 subjects with bipolar disorder type II in remission. In this study population, comorbid personality disorder was a risk factor for an earlier onset of the mood disorder and a higher rate of past suicidal ideation.

Colom et al.[28] conducted a naturalistic study, which evaluated the medication compliance of 200 bipolar outpatients during a 2-year period. This study showed that the subjects with a comorbid Axis II disorder had higher rates of poor medication compliance and higher numbers of hospitalizations. Bieling et al.[57] conducted a naturalistic study that followed 87 bipolar (type I and II) outpatients in various mood states for 12 months. The SCID-II questionnaire (DSM-IV version) was used to screen for personality disorders. The group with best clinical outcome had fewer personality disorder symptoms in 7 out of 10 disorder categories compared to the 2 groups with worse clinical outcome.[57] Swartz et al.[58] reported a prospective case control study, which compared the illness course of 58 bipolar I patients with 12 patients with bipolar I and borderline personality disorder. All the sub-

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jects were in a mood episode at the start of the study. The study found that the median time to stabilization for the comorbid group was 95 weeks, compared to 35 weeks in the bipolar-only group. Additionally, the comorbid group needed significantly more atypical mood-stabilizing medications than the bipolar-only group.[58]

Dunayevich et al.[59] studied 59 bipolar patients hospitalized for mania or a mixed episode. After assessment for personality disorders near the time of discharge, the subjects were then reevaluated at 2, 6, and 12 months after discharge to assess for mood symptoms and functional recovery. Survival and logistic regression analyses from this study showed that subjects with a personality disorder were significantly less likely to achieve symptomatic and functional recovery.[59] Carpenter et al.[22] measured symptom course and social functioning in their study of 23 married bipolar patients. Symptom course was measured by the Brief Psychiatric Rating Scale (BPRS) between 6 to 24 months. Subjects with personality disorders had higher BPRS scores. Social functioning was assessed by the subjects as well as their spouses. The ratings by subjects and spouses indicated that subjects with personality disorders had poorer social functioning.[22]

Hammen et al.[60] studied the clinical and psychosocial predictors of work adjustment in 52 bipolar I subjects over a 2-year period. Their results indicated that personality disorder symptoms and social functioning significantly predicted work functioning after clinical variables were accounted. A study by Loftus and Jaeger[31] studied 51 bipolar I subjects approximately 1 year after a psychiatric hospitalization. This study measured functional outcome in 3 domains: occupational, residential, and social. The authors found that in all 3 domains comorbid personality disorders and maladaptive personality traits were associated with impaired functioning. However, these relationships were not independent of current mood symptoms.[31]

McGlashan[61] provided the only study on the long-term effects of comorbid personality disorder on the illness course of bipolar disorder. In this study, 33 bipolar patients who had been diagnosed with personality disorder were compared to 33 bipolar patients without personality disorder. The outcome measures after 15 years showed a higher rate of alcohol abuse in the cohort with personality disorder, although there was no difference in other outcome measures.[61] The association of bipolar disorder, Axis II pathology, and alcohol abuse is consistent with the findings of Kay et al.[25]

THE IMPACT OF PERSONALITY FACTORS IN TREATMENT RESPONSE TO MEDICATIONS

Several studies have investigated the effects of comorbid personality disorder and maladaptive personality traits on the treatment response of bipolar patients to mood stabilizing medication. In the study by Gaviria et al.,[55] comparing bipolar patients with and without borderline personality disorder, the borderline group had poorer compliance with lithium and had to be terminated earlier from the study compared to the non-borderline group. In a study of 20 bipolar adolescents,[16] the subjects with Axis II diagnoses were less responsive to lithium and required more neuroleptic medication compared to the subjects without personality disorder. Gasperini et al.[19] followed 54 bipolar disorder subjects on long-term lithium treatment. All subjects were compliant with lithium treatment as confirmed by serum levels. In this study, the presence of a personality disorder was associated with increased measures of illness recurrence.[19] In the study by Calabrese and colleagues,[35] multiple regression/discriminant analyses were done to evaluate predictors of therapeutic response to valproate for 101 rapid cycling bipolar subjects. Twenty-seven percent of the subjects had a diagnosis of borderline personality disorder, and the presence of borderline personality disorder predicted a negative outcome.

Abou-Saleh[62] studied 53 bipolar subjects who had been on lithium prophylaxis for 6 months. The subjects were divided into a lithium responders group (29 subjects) and a nonresponders group (24 subjects). Responders were defined as those who had no recurrence of affective episodes after 6 months of starting lithium treatment. Nonresponders were defined as those having at least 1 mood episode after the first 6 months of lithium prophylaxis. All subjects completed the Eysenck Personality Questionnaire and Foulds' Personality Deviance Scale while euthymic. The Eysenck Personality Questionnaire measures the personality dimensions of psychoticism, extraversion, and neuroticism. The Foulds' Personality Deviance Scale measures dimensions of intropunitiveness, extrapunitiveness, and dominance. The results showed that lithium nonresponders were more deviant from normative measures than lithium responders on neuroticism and dominance.[62] Maj et al.[63] also used the Eysenck Personality Questionnaire to study 51 bipolar and 49 unipolar depressive subjects. All subjects were treated for 2 years with lithium at therapeutic levels. The subjects were divided into lithium responders and nonresponders. Nonresponders were defined as those who had 1 or more relapses needing hospitalization or addition of antidepressants or antipsychotics. This study also found an association between high neuroticism scores and poor response to lithium.[63]

DISCUSSION

Studies have investigated the relationship of bipolar disorder and personality using many different research instruments and designs. The widely different methods and sample sizes of these studies make comparison, statistical meta-analysis, and formation of conclusions extremely difficult. Any research involving personality measures is

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fraught with inherent difficulties described in the introduction. In the comorbidity studies, both inpatient and outpatient bipolar samples were consistently found to have a prevalence of Axis II psychopathology much higher than that of the population (5.9%–17.9%[25]). This finding may partly result from sampling from clinical populations, some from tertiary care centers. This sampling bias limits our ability to generalize the modest findings of this review article. The review of comorbidity studies also found a wide range of prevalence rates in both inpatient and outpatient studies. The authors of this review hypothesized that at least a trend would emerge with inpatient comorbidity rates higher than outpatient rates given the relative mood stability of outpatient bipolar subjects compared to inpatient subjects. However, this trend did not emerge when the comorbidity rates of the studies in both groups were averaged (after being weighted for sample size). A comparison of the inpatient studies[32,43–45] using structured interviews to the outpatient studies[19,20,22–26,28] using structured interviews with euthymic subjects produces only a modest difference in comorbidity rates (45.8% vs. 37.7%).

Several factors should be considered when reviewing the summarized results of the comorbidity studies. Most of the studies are limited by relatively small sample sizes. More importantly, the interrater reliability of the research instruments used in different studies varies considerably. One study[5] found the interrater reliability of the PDE and SIDP-R to be lower than later studies of the SCID-II. Only through intensive rater training and rater counterbalancing measures did the reliability of personality disorder diagnosis improve. Another factor that complicates the analysis of the prevalence studies is the systemic changes from managed care during the period of the studies. Criteria for hospital admission and models of outpatient care changed, resulting in more symptomatic patients being treated in outpatient settings.

Several findings from a review of the outpatient comorbidity studies are noteworthy. Firstly, the 2 studies that found the highest prevalence rates of personality disorders did not control for mood state at the time of diagnostic interview.[18,21] These studies found the prevalence rate to be 84.0% and 70.3%, respectively, compared to an average of 37.7% in the 8 outpatient studies with euthymic subjects. This finding suggests a relationship between mood instability and more severe personality disorder symptoms despite the lack of evidence found in comparing the inpatient and outpatient prevalence data. Another finding from a review of the outpatient studies is the tendency of self-report personality measures to diagnose personality disorders at a higher rate than structured interviews. The 2 studies that used self-report questionnaires[17,25] found the prevalence rate of Axis II disorders in bipolar disorder to be higher (62% and 58%, respectively) compared to the average prevalence of 37.7% found in the 8 studies that administered structured interviews to subjects in full remission. This finding is consistent with those of non-bipolar studies that have used self-report personality instruments or investigated their validity.[37–39] Conversely, the 2 prevalence studies that conducted retrospective chart reviews[42,46] showed relatively low rates (23% and 9%, respectively) of Axis II comorbidity in bipolar patients.

The authors of this review hypothesized that cluster B personality disorders will be found more commonly in bipolar patients than other Axis II disorders given the similarity of some symptoms. One inpatient[32] and 3 outpatient[19,24,29] studies found histrionic personality disorder the most common comorbidity. However, no consistent results emerged in regard to the most common personality disorders found in bipolar disorder. Several studies were found that indicated a more virulent course of illness in bipolar patients with cluster B personality disorders.[36,53,55]

In the studies that measure personality traits rather than DSM-defined personality disorders, bipolar patients often show higher rates of abnormal personality traits compared to normative samples.[47,48,50] These studies also indicate that abnormal personality traits are associated with a worse course of illness.[49,51] Studies that have explored the illness course of bipolar disorder have found that comorbid personality disorders are associated with a lower medication compliance rate, lower rate of clinical recovery, lower functional level, higher rates of suicidality, and higher rates of substance abuse.[25,26,28,29,36,53–61] The studies on treatment response also indicate that a comorbid personality disorder and abnormal personality traits predict a poorer response to lithium and valproate.[16,19,35,55,62,63] These findings are consistent with the emerging literature on the clinical impact of Axis II comorbidity on other disorders. For example, studies in major depressive disorder have shown that comorbid Axis II disorders are associated with chronicity, poorer response to medication, longer time to treatment response, higher rates of relapse, and shorter time to recurrence.[64–66]

Very few studies can be found that discuss the effective management of bipolar disorder with comorbid personality disorder.[67] It would be reasonable to suggest that a multi-modal and intensive management strategy will be needed to stabilize these patients with complex psychopathology. Along with aggressive pharmacotherapy to stabilize mood, psychotherapy may be needed to address Axis II disorders. Psychodynamic therapies have been the traditional approach to treat personality disorders.[68–72] More recently, cognitive-behavioral strategies have been successfully applied to the treatment of borderline personality disorder in the form of dialectical behavioral therapy.[73] Resources such as intensive case management and partial hospital and mobile outreach programs should be considered to prevent poor treatment outcomes in this comorbid population.

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Further research on the comorbidity of personality disorders in bipolar disorder is encouraged to clarify the relationship of personality and mood psychopathology. Longitudinal studies that investigate the long-term effects of this comorbidity are needed. Only 1 study was found in this review that addresses this topic.[61] Longitudinal studies can also provide evidence as to which treatment strategies are more effective for bipolar patients with Axis II comorbidity. The authors of this review were disappointed to discover only 2 studies[26,27] on Axis II comorbidity in bipolar disorder type II. The scarcity of studies on this topic prevents a useful comparison of the effects of personality pathology in bipolar I and bipolar II disorder. More studies are needed to study the effects of Axis II comorbidity on specific bipolar populations such as bipolar II, rapid cycling, treatment resistant, and male/female patients. Most of the studies reviewed in this article have relatively small sample sizes. Larger studies using standardized, validated measures of personality pathology may provide a better understanding of which personality disorders are more common and have the most effect on illness course and treatment response in bipolar disorder.

Drug name: lithium (Lithobid, Eskalith, and others).

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