

REVIEW ARTICLE

Personality disorders in euthymic bipolar patients: a systematic review

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Objective: To identify, by means of a systematic review, the frequency with which comorbid personality disorders (PDs) have been assessed in studies of euthymic bipolar patients.

Methods: PubMed, SciELO and PsychINFO databases were searched for eligible articles published between 1997 and 2013. After screening 1,249 empirical papers, two independent reviewers identified three articles evaluating the frequency of PDs in patients with bipolar disorders assessed in a state of euthymia.

Results: The total sample comprised 376 euthymic bipolar patients, of whom 155 (41.2%) had at least one comorbid PD. Among them, we found 87 (23.1%) in cluster B, 55 (14.6%) in cluster C, and 25 (6.6%) in cluster A. The frequencies of PD subtypes were: borderline, 38 (10.1%); histrionic, 29 (7.7%); obsessive-compulsive, 28 (7.4%); dependent, 19 (5%); narcissistic, 17 (4.5%); schizoid, schizotypal, and avoidant, 11 patients each (2.95%); paranoid, five (1.3%); and antisocial, three (0.79%).

Conclusion: The frequency of comorbid PD was high across the spectrum of euthymic bipolar patients. In this population, the most common PDs were those in cluster B, and the most frequent PD subtype was borderline, followed by histrionic and obsessive-compulsive.

Keywords: Bipolar disorder; affective disorder; mood disorder; personality disorders; comorbidity

Introduction

Bipolar disorders (BD) are a group of chronic and recurrent diseases characterized by pathological mood changes. The lifetime prevalence of BD types I and II in the general population is approximately 2%, and sub-syndromal forms of BD affect at least a further 2%.¹ Even with treatment, about 37% of patients experience recurrence of mania or depression within a year, and 60% within 2 years.² In the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study, with a cohort of 1,469 participants, 58% of patients with BD type I and II achieved full recovery, but 49% had recurrences in a 2-year interval. These relapses were twice as frequent in patients with negative polarity as in those with positive polarity.³ In fact, patients with BD may experience residual depressive symptoms during, on average, one-third of all days of their lives.⁴

Bipolar patients also experience functional impairment in various forms, low levels of quality of life, and the possibility of being stigmatized.⁵ Part of these losses are

also due to high rates of comorbidity with psychiatric axis I and II disorders, with therapeutic and prognostic implications.^{6,7} Among the comorbidities of greater impact in patients with BD are personality disorders (PDs). Several studies have shown that the co-occurrence of BD and PD generates a negative impact on response to treatment, increased suicidal behavior, and reduced global functioning in bipolar patients.⁸⁻¹¹

According to DSM-IV and DSM-5, PDs can be divided into three groups on the basis of clinical similarities: group A (paranoid, schizoid, and schizotypal), group B (antisocial, borderline, histrionic, and narcissistic), and group C (avoidant, dependent, and obsessive-compulsive).^{12,13} Despite being among the most prevalent mental disorders in the general population, affecting 10 to 23% of all persons,^{14,15} PDs continue to be under-investigated, and large information gaps persist regarding their epidemiology and their relationship with BD.¹¹

In general, rates of PD comorbidity in patients with BD reach 25-50%,¹⁶⁻²⁰ according to recent studies. Nevertheless, rates up to 73.6%^{21,22} have been found, especially when evaluating hospitalized or highly symptomatic patients. Additionally, variability may also be due to methodological differences, such as instruments used, phase of the disease at the time of data collection, and criteria for euthymia. In fact, studies evaluating symptomatic patients have shown that depressive or manic

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symptoms alter self-perception, and therefore can generate misleading rates of comorbid PD.²³ Thus, to avoid diagnostic errors by misperception of certain personal characteristics or overlapping symptoms, the presence of psychiatric comorbidity in BD patients should preferably be evaluated while they are in a euthymic state.²⁴

The controversy over these issues notwithstanding, negative outcomes are worse in bipolar patients with comorbid PD. Therefore, PD should be investigated in any treatment plan. In an attempt to identify the frequency of PD in bipolar patients with greater accuracy, we conducted a systematic review of the literature on the frequency of PD in BD type I, BD type II, cyclothymia, or BD not otherwise specified (NOS), restricted to assessments performed in a state of euthymia, according to DSM-IV diagnostic criteria. The rates observed in BD patients were then compared to rates of PD in the general population to identify differences between these two groups.

Methods

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA guidelines),²⁵ we conducted a systematic review of the literature on the frequency of PD in patients with BD assessed only in a state of euthymia, according to the criteria for complete remission found in DSM-IV.¹² The electronic databases MEDLINE, SciELO, and PsychINFO were searched. The basic search strategy for MEDLINE was the query (“bipolar disorder” OR “affective disorder” OR “mood disorder”) AND (“personality disorders” OR “axis II”) AND (“comorbidity” OR “comorbid”). The searches conducted in the other databases were analogous. Additional studies were obtained by hand-searching the references of selected articles. The search was limited to articles written in Portuguese, English, Spanish, and Italian and published between 1997 – the year of publication of the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) – and December 31, 2013.

The eligibility criteria for the review were: studies that assessed the frequency of PD in adults (≥ 18 years old) of both genders with BD type I, II, cyclothymia, or BD NOS, according to DSM-IV criteria, during a period of at least 2 months in which there was no sign or symptom of mania or depression. Clinical trials and cross-sectional, prospective and retrospective studies were included, as long as frequency of PD in BD patients was one of the outcomes of the study at any time. To homogenize the diagnostic criteria for PD, we selected only articles that evaluated all 10 specific types of PD and PD-NOS using the SCID-II, which is considered the gold-standard instrument for this purpose. Furthermore, studies were required to use scales to rate the intensity of mood symptoms that indicated remission of symptoms at the time of evaluation (Hamilton Depression Rating Scale [HAM-D] ≤ 8 ; Young Mania Rating Scale [YMRS] ≤ 7). We did not exclude studies on the basis of sample size.

Considering the eligibility criteria, two authors (SBF and FLL) independently reviewed the titles and abstracts of the retrieved studies and selected items for full-text reading. Divergences in item selection were resolved by consensus. The selected studies were evaluated with respect to study methods, type of study design, psychometric instruments, diagnostic criteria, subjects, setting, outcome variables, and results.

Sample characteristics and the frequency of bipolar patients with at least one PD were collected from each article. One author extracted the data (FLL), and the other checked the extraction (SBF). On the basis of these data, the frequency of PD for the total sample was calculated. However, the frequencies of each PD were calculated separately, because patients could have more than one disorder.

Results

Overall, the database searches and hand-searches of the references of relevant manuscripts yielded 1,249 citations, 12 of which were deemed potentially relevant. Further examination of these articles was performed and yielded a final sample of three eligible articles. The remaining nine articles were excluded because they did not meet the inclusion criteria: four studies mixed inpatients and outpatients^{10,26-28}; two included only hospitalized patients^{20,22}; and the remaining three included outpatients, but not all were in euthymia.²⁹⁻³¹ Most of the studies used diagnostic scales other than HAM-D and YMRS, and some used none at all (Figure 1).

The three selected studies were conducted in outpatient services of European universities, on patients with BD type I, II, and cyclothymia (Table 1). No study of BD-NOS was found. The total sample comprised 376 patients, of whom 155 (41.2%) had at least one comorbid PD. Among them, 87 (23.1%) belonged to cluster B, 55 (14.6%) to cluster C, and 25 (6.6%) to cluster A. The most frequent PD subtypes were borderline ($n=38$, 10.1%), histrionic ($n=29$, 7.7%) and obsessive-compulsive ($n=28$, 7.4%), followed by dependent ($n=19$, 5%), narcissistic ($n=17$, 4.5%), schizoid, schizotypal, and avoidant ($n=11$ each, 2.95%), paranoid ($n=5$, 1.3%), and antisocial ($n=3$, 0.79%). Seven patients (1.86%) had PD-NOS (Table 2).

Discussion

To our knowledge, this is the first systematic review of the literature to describe the frequency of PD in patients with BD assessed only in a state of euthymia. As noted in this review, there is a vast literature on the association between PD and BD. However, few studies have evaluated comorbid PD in bipolar patients during remission of symptoms using appropriate instruments for diagnosis of PD to minimize potential measurement bias, such as interpreting affective symptoms as dysfunctional personality traits. Thus, the studies selected for this review included only patients defined as euthymic according to DSM-IV criteria, using scales of intensity of affective symptoms, which strongly suggest the absence of acute

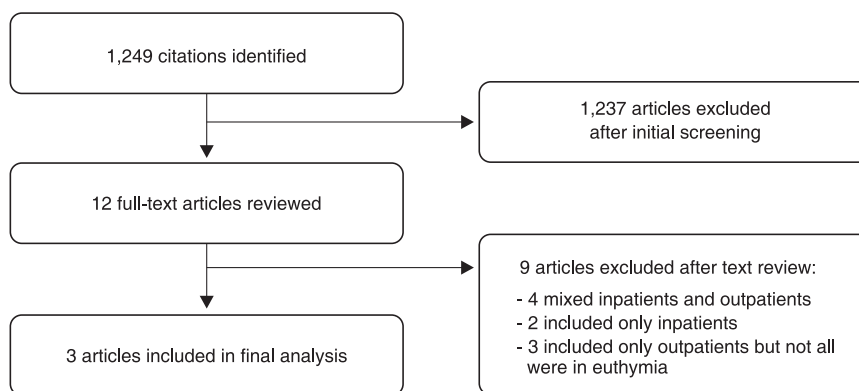


Figure 1 Flow chart of the search strategy

or subsyndromal states for personality assessment. Furthermore, to ensure adequate characterization of PD, we selected articles which used only the SCID-II and included all 10 specific types of PD as well as PD NOS.

Despite methodological accuracy in the selection of papers, this review found a high frequency of axis II disorders in subjects with BD; 41.2% of patients had at least one PD. This high rate is similar to that found in a recent systematic review (42%) that included studies with patients in different symptomatic states and used different diagnostic methods.³⁴ However, the aforementioned review included many studies of probably euthymic outpatients, which may have led to the similar rates of comorbid PD. Likewise, similar rates were also described in the few previous studies that evaluated only euthymic patients employed the SCID-II version based on DSM-III,³⁵ thereby precluding similar characterization between the different types of PD.

The DSM-III listed 11 specific types of PD, 10 of which were maintained in DSM-IV and DSM-5. Specifically, the disorder recognized as passive-aggressive PD in DSM-III was placed under PD NOS in the more recent versions. Moreover, DSM-IV and DSM-5 differ from DSM-III in diagnostic criteria, especially in groups B and C. For example, in antisocial PD, the total number of diagnostic criteria decreased from 10 to seven, and the minimum number of items for diagnosis was reduced from five to three. In borderline PD, a ninth criterion was added: "transient, stress-related paranoid ideation or severe dissociative symptoms." Furthermore, the number of items required to make the diagnosis of histrionic PD was reduced from five to four, along with other changes such as replacing the criterion "is self-centered, actions

being directed toward obtaining immediate satisfaction; has no tolerance for the frustration of delayed gratification" with "is suggestible (i.e., easily influenced by others or circumstances)."^{12,13,36}

With respect to cluster C, dependent and obsessive-compulsive PD were the only disorders to undergo changes in conceptualization and number of diagnostic criteria.

According to Friberg et al., studies based on different classification systems influence the diagnosis of PD in patients with comorbid mood disorders. Those which use the DSM-III-R have been found to produce higher frequencies of PD than those based on DSM-IV, reinforcing the importance of the adoption of uniform criteria for diagnosis of PD, as adopted in this review.³⁴

Despite the changes in DSM diagnostic criteria mentioned above and the possible difference in the frequency of PD diagnosis between versions, studies using the DSM-III-R in euthymic patients have found higher rates of PD: 25.6 to 47.7% of patients with BD type I^{17,18} and 32.5% of patients with BD type II.¹⁹

The studies selected for the present review also reported differing results. In the study by Harnic et al., 61.5% of PD patients had BD I, 15.3% had BD II, and 23% were cyclothymic.³³ On the other hand, Rosso et al. found no significant difference in the frequency of PD between patients with BD type I and BD type II (43.7 vs. 41.7% respectively).²³ The criteria for both studies were similar as to duration of euthymia, but Rosso et al. used stricter criteria for affective symptom scores (HAM-D \leq 7 and YMRS \leq 6 to define euthymia), and this methodological difference could partially explain the difference between their results. The third study reported

Table 1 Characteristics of included studies

Article	n	Sample	Scales	Frequency (%)	Personality disorder
Colom ³²	120	BD type I, II	HAM-D \leq 7 YMRS \leq 5	31	Borderline, histrionic, OCPD
Rosso ²³	186	BD type I, II	HAM-D \leq 7 YMRS \leq 6	42.5	OCPD, borderline, narcissistic
Harnic ³³	70	BD type I, II, cyclothymic	HAM-D \leq 8 YMRS \leq 7	55.7	Borderline, histrionic, narcissistic

BD = bipolar disorder; HAM-D = Hamilton Depression Rating Scale; OCPD = obsessive-compulsive personality disorder; YMRS = Young Mania Rating Scale.

Table 2 Frequency of personality disorders in euthymic bipolar patients

Personality disorder	n (%)
Borderline	38 (10.1)
Histrionic	29 (7.7)
Obsessive-compulsive	28 (7.4)
Dependent	19 (5.0)
Narcissistic	17 (4.5)
Schizoid	11 (2.9)
Schizotypal	11 (2.9)
Avoidant	11 (2.9)
Paranoid	5 (1.3)
Antisocial	3 (0.8)
Not otherwise specified	7 (1.9)

Numbers and percentages do not add up to total amounts because some subjects had more than one disorder.

a 31% rate of PD, but did not differentiate between BD subtypes.³²

Another important aspect concerns the subtypes of PD clusters. Fan & Hassell developed the hypothesis that, due to the similarity of some symptoms, cluster B disorders are more commonly found in bipolar patients than clusters A and C.¹¹ Regardless of the instruments used and the symptomatic state in which patients are evaluated, cluster B disorders remain those most frequently reported.^{22,27,33,34} In our review, 87 patients (23%) belonged to this cluster, confirming the existing literature.

Distinguishing between trait and state in the presence of affective episodes – and hence, defining comorbidity with cluster B PDs – is challenging. The temporal delimitation of symptoms plays a crucial role in this distinction. For example, symptoms such as impulsivity, aggression, and reckless disregard for safety can be seen in both antisocial PD and in mixed states. Likewise, the grandiosity and presumptuous behavior present in narcissist PD can be confused with symptoms of hypomania.¹¹ However, affective symptoms have limited duration, whereas dysfunctional personality traits begin early in adolescence and persist over time, regardless of the state of mood.

Furthermore, the distinction between symptoms of BD and those of borderline PD can be particularly difficult to identify. Since the introduction of borderline disorder in DSM-III,³⁵ the overlap of diagnostic criteria and the presence of clinical similarities between borderline PD and BD has rendered the existence of the former controversial to some scholars.³⁷ Both disorders may feature a history of childhood abuse, self-harm, intermittent paranoia, mood instability, sleep disorders, and depressive episodes with atypical symptoms.^{11,38} In our review, borderline PD was the most frequent comorbid PD in bipolar patients, with a rate of 10%, tenfold that observed in the general population.³⁹ However, reported rates varied broadly, ranging from 6.2 to 30% in BD type I,^{17,19-21,40} and 12 to 23% in BD type II.^{16,41,42}

On the other hand, comorbid antisocial PD was very infrequent in the studies included in our review (0.79%), and seems to be more common in BD type I than in type II.³⁹ In the general population, the prevalence of antisocial

PD can be up to five times higher (4.1%) than that found in this review.⁴³

Although cluster A disorders are the second most prevalent PDs in the general population (1.6 to 6.2%),⁴³⁻⁴⁵ they are less frequent among BD patients. Our review found a 6.6% frequency of cluster A PDs in this group, which is very similar to the prevalence in the general population. This fact may be attributable to there being little overlap between the diagnostic criteria of cluster A disorders and BD when patients are evaluated in euthymia.

Cluster C is the most prevalent of the PD clusters in the general population (2.4 to 6.8%), and was substantially frequent in bipolar patients (14.6%) in this review. Among the cluster C disorders, obsessive-compulsive PD is one of the most common in both the general population (2.1 to 7.9%) and in BD patients (7.4%).⁴³⁻⁴⁵

Contradicting our results, Friborg et al. found almost twice the rates of cluster A and C disorders as in our review (cluster A: 13 vs. 6.6%; cluster C: 26 vs. 14.6%). Interestingly, in their review, avoidant and paranoid PD were among the most frequent comorbid disorders, with rates four and eight times higher than those found in our analysis (avoidant: 12 vs. 2.95%; paranoid: 11 vs. 1.3%). Moreover, histrionic PD, which ranked second in our analysis (7.7%), was only the sixth most common PD (10%) in the Friborg et al. review.³⁴ These differences in the frequencies of some specific PDs and of certain clusters may be partially explained by methodological differences between studies.

Even as controversy remains over rates of comorbid mood disorders in PD, there is no denying their high overall frequency in patients with bipolar disorder and their negative impact on treatment and outcomes in this population, as PDs may be implicated in self-harm, substance abuse, and patient difficulty in recognizing improvement of BD manifestations, and may influence the development of the therapeutic alliance for treatment compliance.^{8,46-48}

With respect to treatment, although antipsychotics and mood stabilizers seem to improve global functioning in patients with borderline and/or schizotypal PD,⁴⁹ few studies have addressed concurrent medical and psychological treatment in bipolar patients with comorbid PD. In this context, lamotrigine and valproate may alleviate symptoms of both BD and borderline PD,⁵⁰ and psychoeducation seems useful as an adjunctive treatment in the prophylaxis of BD with any comorbid PD.³² In patients not receiving concurrent combination treatment, stabilization of a mood episode should be followed by efficacious adjunctive treatment for the PD, such as dialectical behavior therapy or transference-focused therapy for borderline PD.^{48,51}

In short, even in the absence of clear evidence regarding best therapeutic practices in dealing with the association of each PD and BD, any BD treatment plan should include a thorough investigation for the presence of PD, especially in patients who do not respond to first-line psychopharmacotherapy for BD. Adequate medical and psychological assistance can help patients cope better with their behavior and achieve a better prognosis,

with the possibility of exhibiting less comorbidity through longitudinal follow-up.⁴⁸

One limitation of this study is the small number of articles included in the final analysis. Furthermore, the fact that all were conducted in Europe impedes generalization of results.

In conclusion, despite controversy about the comorbid occurrence of PD and BD, this review found a high frequency of PD (41.2%) in bipolar patients assessed only during euthymia. In these patients, the most common PDs were those belonging to cluster B (23.1%), followed by cluster C (14.6%) and cluster A (6.6%). The most frequent specific PDs were borderline (10.1%), histrionic (7.7%), and obsessive-compulsive (7.4%) PD.

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Disclosure

The authors report no conflicts of interest.

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