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Comorbidity between bipolar disorder and cluster B personality disorders as indicator of affective dysregulation and clinical severity

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Introduction: Several lines of evidence have well established a relationship between Bipolar Disorder and Cluster B Personality Disorders. The study compares mood spectrum and temperamental symptoms, personality traits and clinical characteristics among outpatients (n = 63) diagnosed with major depression (MD), bipolar disorder (BD), cluster B personality disorders (PD-B) and comorbidity of BD + PD-B.

Method: The diagnosis was determined with structured interviews (MINI and SCID II) and symptom assessments with evaluation and diagnostic instruments (MOODS-SR, BI, TEMPS-A and IPDE). Differences between groups were explored with *post hoc* analysis and analysis of variance.

Results: Patients with BD+PD-B comorbidity presented an earlier onset and more severity in suicide attempts, hospitalizations and self-harm behaviors. They showed more characteristics of cyclothymic and irritable temperament and more cluster A and B personality traits, than patients with BD only. PD-B patients obtained intermediate scores in manic like symptoms: higher than patients with depression and lower than patients with bipolar disorder. However, the Bipolarity Index clearly distinguished patients with BD or with comorbidity (BD+PD-B) from the other diagnostic groups (PD-B and MD).

Conclusions: BD+PD-B comorbidity presents a more severe type of emotional dysregulation compared to the other diagnostic groups, including BD and PD-B alone. Assessing temperament, personality traits, emotional dysregulation in mania and depression, self-harm and hospitalizations severity and age onset could facilitate differential diagnosis and enhance effectiveness of treatments for BD, PD-B and their comorbidity.

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Keywords: Bipolarity, Affective disorders, Cluster B personality disorders, Borderline personality, Comorbidity in bipolarity

Actas Esp Psiquiatr 2013;41(5):269-78

La comorbilidad del trastorno bipolar con trastornos de la personalidad tipo B como indicador de severidad clínica y desregulación afectiva

Introducción: Varias líneas de evidencia han establecido una relación entre el Trastorno Bipolar y los Trastornos de la Personalidad del grupo B. El estudio compara los síntomas del espectro del ánimo, temperamentales, de personalidad y características clínicas entre pacientes ambulatorios (n=63) diagnosticados con Depresión Mayor (DM), Trastorno Bipolar (TB), Trastornos de la Personalidad del grupo B (TP-B) o comorbilidad de TB+TP-B.

Metodología: El diagnóstico se realizó con entrevistas estructuradas (MINI y SCID II), las evaluaciones con instrumentos de evaluación y diagnóstico (MOODS-SR, BI, TEMPS-A y IPDE). Se analizaron diferencias entre grupos con análisis de varianza y análisis *post hoc*.

Resultados: Los pacientes con comorbilidad TB+TP-B presentaron una aparición más temprana y mayor severidad en síntomas, intentos de suicidio, internaciones y autolesiones. Mostraron más características de temperamento ciclotímico e irritable y más rasgos de la personalidad del grupo A y B que los pacientes con TB únicamente. Los pacientes TP-B obtuvieron puntajes intermedios en síntomas maníacos: mayor que pacientes con depresión y menor que pacientes con trastorno bipolar. Sin embargo, el Índice de Bipolaridad claramente distinguió a pacientes con TB solamente o comorbilidad (TB+TP-B) de los otros grupos de diagnóstico (TP-B y DM).

Conclusiones: La comorbilidad TB+TP-B presenta un tipo de desregulación emocional más severa que los demás grupos, incluyendo al TB y el TP-B por sí solos. Evaluar el

temperamento afectivo, rasgos de personalidad, desregulación emocional en la manía y depresión, gravedad de autolesiones, internaciones y edad de inicio, facilitaría el diagnóstico diferencial y la eficacia de tratamientos para TB, TP-B y comorbilidad.

Palabras clave: Bipolaridad, Trastornos afectivos, Trastornos de la personalidad del grupo B, Trastorno límite de la personalidad, Comorbilidad en bipolaridad

INTRODUCTION

The relation between bipolar disorder (BD) and cluster B personality disorders (PD-B) has been extensively debated, mainly due to the symptomatic overlapping between BD and borderline personality disorder (PD).[1,2] At present, the classification of personality disorders has not yet been shown to be satisfactory to either researchers or clinicians. Some authors even question the usefulness of the existence of Axis II as they consider that Axes I and II are state and trait characteristics, respectively, of the same psychopathologic phenomenon.[3] This argument weighs so heavily that it was a decisive factor for classification in the fifth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5).[4]

The way that personality disorders have been classified has been controversial since Axis II was introduced in the DSM.[5] At present, borderline PD is the most studied Axis II disorder in general and cluster B PD is the most studied Axis II disorder in particular. In recent decades, the inclusion of borderline PD as a variant of mood disorders has been debated.[2,6] There have thus been two main proposals for classification. One proposal holds that borderline PD is a variant of bipolar spectrum disorders, whereas the other argues that borderline PD should remain a distinct entity from that classification. Both lines of research have been endorsed by scientists and explored in numerous studies, some arguing for the inclusion of borderline PD in the bipolar spectrum[7-9] and others for the exclusion and clear differentiation of the two disorders.[10-12] However, the evidence found in studies conducted from both positions is inconclusive about the unique identity of each disorder.[13]

Research on the overlap and differentiation of borderline PD and mood disorders has yielded different findings. It has been reported, in supposedly "over-diagnosed" patients with BD (according to DSM-IV criteria[14]), that the diagnosis of borderline PD is significantly more likely when compared to a population with no over-diagnosis of affective disorder.[15] Furthermore, under-diagnosis and delayed detection of bipolar disorders have been reported in various contexts.[16-19] Some authors have postulated that the diagnosis of personality disorders contributes, in many cases, to delayed recognition or erroneous diagnosis of patients with BD.[20,21] Recently, Zimmerman et al.[22] reported that evaluation with the instrument most commonly used to detect bipolar disorders, the Mood Disorder Questionnaire (MDQ),[23] indicates the presence of borderline PD as well as BD, meaning that the evaluation is positive for both disorders. The problem of differentiating borderline PD from mood disorders apparently involves screening instruments as well.

The importance of the above-mentioned controversy is the impact that it has on clinical practice, treatment and research.[24] Despite the apparent impasse in the debate about differentiating conditions, in recent years some studies have shed light on how to resolve the dilemma. Analysis has begun on BD and borderline PD comorbidity as a subgroup, independent of its two component disorders.[25] The study of comorbidity is a concrete alternative that may help to bridge the two main positions. Comorbidity is beginning to be explored as a syndrome in itself, based on the idea that the component conditions could share a common etiology. There has even been discussion of the differential elements found between people with BD + borderline PD and those with either BD alone or borderline PD alone. This approach has made it possible to understand how the symptoms of BD and borderline PD overlap as a result of the interaction of biological and environmental factors.[2,4]

Although the multiaxial classification of DSM-IV allows the joint diagnosis of personality disorders and mood disorders, the internal and external validity of personality disorders has been questioned as independent of Axis I disorders.[26] Beyond the current diagnostic classification, it is necessary to evaluate the elements of the two disorders that differentiate them or are similar. This approach would help to clarify doubts about the future taxonomy and facilitate pharmacologic and psychosocial treatment, as it targets specific behaviors and dimensions rather than general diagnoses.[25]

The aim of this study was to analyze patients with mood disorders (BD and major depression [MD]), cluster B personality disorders (PD-B) and comorbidity (BD + PD-B) with instruments that assess cognitive, affective and behavioral elements of mood and thus detect distinctive characteristics of the diagnostic groups. We proceeded by assessing the characteristics of the affective temperament, personality traits, and symptoms of the bipolar spectrum and mood spectrum of patients, in addition to demographic and clinical characteristics. The subsequent aim was to identify differential markers in BD + PD-B comorbidity to contribute to advancing the differential diagnosis and clarification of the debate on the overlap between affective disorders and cluster B personality disorders.

METHODOLOGY

Sample

A total of 63 outpatients with a diagnosis of major depression (MD, n=9), bipolar disorder (BD, n=12), cluster B personality disorder (PD-B, n=15) and BD + PD-B comorbidity (n=17) were evaluated after giving written informed consent for this study. The sample was recruited by the mental health professionals who were treating patients with a mood disorder and/or cluster B personality disorder. The professionals (psychiatrists and clinical psychologists) were from two private outpatient mental health centers.* The inclusion criteria for participants were: a) age between 18-65 years and capability to understand the objectives and procedures of the study and to give their written informed consent, b) patients meeting diagnostic criteria for depressive, hypomanic, manic or mixed episodes in the present or past according to DSM-IV-TR, including BD-NOS (not otherwise specified), and patients meeting diagnostic criteria for PD-B, c) if the patient has a history of alcohol/substance abuse or dependence, the patient should be in early full remission and abstinent for at least one month before entering the study. Patients were excluded for: a) Axis I psychotic disorder, b) mental disorder of organic cause (mental disorder due to medical causes, such as epilepsy, dementia, stroke and autoimmune diseases), and c) cognitive alterations sufficiently intense to prevent clinical assessment or to obtain consent with adequate understanding of the procedures and objectives of the study.

Procedure

The evaluation process was carried out in two steps. First, the clinician gave the researcher a form with information about the patient, including the Axis I and II clinical diagnosis according to DSM-IV, the Ghaemi-Goodwin[27] criteria for bipolar spectrum, and the Bipolarity Index of Dr. Gary Sachs.[28] At the same time, the patient was given a battery of self-administered scales to complete and return to the researcher. Subsequently, the investigator, blind to the results of the self-administered instruments, conducted a structured neuropsychiatric interview with the patient to screen Axis I and II diagnoses (Mini-international Neuropsychiatric Interview [MINI] and Structured Clinical Interview for DSM-IV Axis II [SCID II], respectively) and record clinical and demographic characteristics. It was verified that at the time of the diagnostic evaluation, the severity of the disorder did not exceed a score of 3 on the Clinical Global Impression for BD (CGI-BD),[29,30] depression and hypomania/mania items.

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Once the data were collected, the total sample (n=63) was divided into four focus groups: MD (n=19), BD (n=12), PD-B (n=15) and BD+PD-B comorbidity (n=17).

Instruments

Participants were assessed with interviewer-administered and self-administered instruments that have been developed and validated in recent years for analyzing affective symptoms and personality traits in each diagnostic group. The instruments used are listed below.

Self-administered instruments

International Personality Disorder Examination, self-administered questionnaire (IPDE)[31] The purpose of this instrument is to identify traits and behaviors relevant to evaluating the diagnostic criteria for personality disorders. The version in Castilian Spanish has demonstrated high sensitivity and moderate specificity.

Mood Spectrum Self-Report Questionnaire (MOODS-SR).[32] This questionnaire is used to evaluate mood symptoms throughout life, traits and lifestyles that characterize syndromic or subsyndromic affective episodes, and temperament characteristics related to mood dysregulation. The 161 items of the questionnaire address three general domains: depression, mania, and rhythmicity. The depression and mania domains are divided into three subdomains: mood, cognition and energy. This instrument makes it possible to differentiate between patients with mood disorders and control patients, and between patients with bipolar depression and unipolar depression, using the score obtained on the global scale and for subdomains. It has also been used to characterize the spectrum of mood phenomenology throughout life.[33-35]

Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A).[36] This instrument is used to analyze emotional temperament traits present throughout life. It consists of 110 items grouped into five dimensional scales of temperament: depressive, cyclothymic, hyperthymic, irritable and anxious. It has been translated, adapted and validated in a sample of patients and controls from the Argentine population.[37]

Structured Clinical Interview for DSM-IV Axis II - self-administered (SCID II).[38] This 119-item questionnaire (closed questions) is divided into groups to evaluate each personality disorder according to DSM-IV criteria. High scores in each group indicate a high likelihood of meeting criteria for PD, which is evaluated later through a semistructured interview.

Bipolar Spectrum Diagnostic Scale (BSDS)[39] and *Mood Disorder Questionnaire (MDQ).*[40,41] These two screening instruments are used to detect bipolar disorder and bipolar spectrum, respectively. The performance of each of these

instruments in this group of patients is explained in another article in preparation**.

Interviewer-administered instruments

Mini-international Neuropsychiatric Interview (MINI).[42] The MINI is a structured interview validated against the SCID and Composite International Diagnostic Interview (CIDI) as a diagnostic tool. It explores criteria for Axis I mental disorders and allows the diagnosis of single or comorbid disorders in the same axis.

Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II).[43] This diagnostic interview has shown internal consistency as a complete instrument and in its component subscales. The version in Castilian Spanish has been validated. The interview shows whether the positive items of the self-administered questionnaire are present with sufficient intensity to meet diagnostic criteria.

Bipolarity Index of Gary Sachs (BI).[28] This is a complementary diagnostic tool for patients with mood disorders. It evaluates features that combine evolution, age at onset, inheritance, response to treatment and characteristics of the mood episodes. The score ranges from 0 to 100. In our clinical sample, we established ad hoc a cutoff point of 50 using a receiver operating characteristic (ROC) curve and calculating the area under the curve (controlling sensitivity and specificity).**

Bipolar Spectrum Criteria of Ghaemi-Goodwin.[27] This instrument consists of three areas of operational criteria that represent characteristics of recurrent depression related to a greater probability of a bipolar type outcome. Spectrum criteria are not used to find a DSM-IV diagnosis of BD, but a probability of evolution and response to bipolar type treatment. The bipolar spectrum criteria evaluate the characteristics of the symptoms, evolution, inheritance and response to antidepressant agents in patients with recurrent depression who have not had spontaneous hypomanic/manic episodes. The instrument has been validated and showed good reliability properties.

STATISTICAL ANALYSIS

The analysis was carried out using nonparametric tests to control for the normal distribution of the sample. Results were obtained by analysis of variance with SPSS, version 16. Using the Kruskal Wallis test, it was possible to detect differences between diagnostic groups in the MOODS-SR , TEMPS-A, IPDE and BI scores, clinical symptoms and demographic characteristics. Analyses were applied post hoc with the Mann-Whitney U test to identify specifically the groups that showed differences between them. Statistical significance was set at $p < 0.05$.

** The analysis will be presented in another study on instruments for the detection of BD: Apfelbaum S, Regalado P, Herman L, Gagliesi, P (in preparation).

RESULTS

The analysis of variance carried out is described in three sections that provide information on the differences between the four diagnostic groups. In first place, there are differences in the spectrum of mood (MOODS-SR) and bipolarity (BI) that subsequently were detected in emotional temperament (TEMPS-A) and, finally, in clinical symptoms and personality traits (IPDE). It is noteworthy that there were no significant differences between groups in terms of sex (x^2=1.488, p=0.69) or educational level (x^2=1.418, p=0.70). Age was significantly younger in patients with PD-B (z=-2.552, p=0.010) and comorbid BD + PD-B (z= -1.936, p=0.041) compared to those diagnosed with MD.

Mood spectrum symptoms and bipolarity traits

We found that people diagnosed with bipolar disorder (BD) had higher scores on the *mania* domain (MOODS-SR) than people with major depression (MD) (z=-2.617, p=0.008). However, there were no significant differences in this respect between people with BD and people with PD-B (z= -0.650, p=0.54). Patients with PD-B had intermediate scores between the MD group and the BD group (means: BD=37.5; PD-B=32.9 and MD=22.8).

The comorbidity group (BD+PD-B) was the group that differed most, showing not only higher scores for manic symptoms (z=-2.445, p=0.014), but also a higher total score on the mood spectrum scale (MOODS-SR) (z=-2.510, p=0.011) and a nonsignificant tendency to score higher on the *depression* and *rhythmicity* domains than people with a diagnosis of MD. The statistical details are shown in Table 1 and the significance of the findings is explained in Figure 1.

On the other hand, we found that the bipolarity index (BI) clearly distinguished between the BD group and the PD-B and MD groups using a cutoff score of 50. The BI identified the patients in our sample with a diagnosis of BD with a specificity of 0.88 and sensitivity of 0.90.

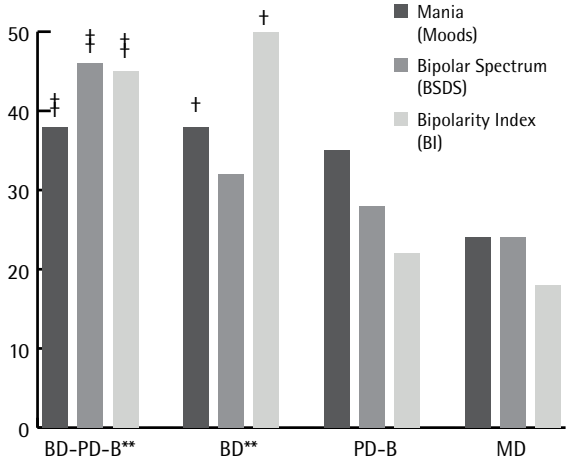
Emotional temperament

Patients with comorbidity had higher scores for cyclothymic temperament on the TEMPS-A than people with PD-B (z=-2.444, p=0.015), BD (z=-2.572, p=0.001) and MD (z=-2.344, p=0.019). In addition, patients diagnosed as having comorbidity (z= -3.478, p=0.001) and patients with PD-B (z=-2.900, p=0.003) had more irritable temperament

Table 1 Differences between diagnostic groups according to mood spectrum symptoms and bipolarity features

MOODS	(Analysis with Kruskal Wallis test) x^2	Diagnostic Groups (Range of mean)			
		BD	MD	PD-B	BD + PD-B
Depression	1.144	31.83	28.74	32.63	35.21
Mood	0.560	29.58	31.82	34.73	31.50
Energy	0.342	32.21	30.10	33.53	32.65
Cognition	2.919	33.79	27.05	30.97	97.18
Mania	7.483*	37.42 †	22.82	32.90	37.65 ‡
Mood	6.621	35.04	23.16	34.47	37.56
Energy	5.968	39.67	24.71	30.80	35.79
Cognition	4.668	37.67	25.00	32.03	35.79
Rhythmicity	3.817	28.17	37.39	31.37	41.68
Total	6.922	35.25	23.26	33.03	38.56 ‡

x^2: Chi-square, BD: bipolar disorder, MD: major depression, PD-B cluster B personality disorder,
BD+PD-B: Bipolar disorder and cluster B personality disorder comorbidity.
* The difference is significant to p<0.05 / ** The difference is significant to p<0.01.
† Comparison between groups using the Mann-Whitney U test: BD>MD, statistically significant, p<0.01.
‡ Comparison between groups using the Mann-Whitney U test: BD + PD-B> MD, statistically significant, p<0.05.



† Patients with comorbidity (BD+PD-B) showed significantly more symptoms and mood spectrum criteria than the MD group.

‡ Patients with bipolar disorder (BD) had much more manic symptoms than patients with depression (MD) (z=-2.617, p=0.008) but did not differ significantly from patients with cluster B personality disorders (PD-B) .

The bipolarity index (BI) distinguished BD from the PD-B and MD groups without detecting large differences with respect to the comorbidity group.

Figure 1 *Significant differences in bipolar aspects among diagnostic groups*

traits compared to patients diagnosed as having BD alone. This indicates that irritable temperament may be a factor more typical of PD-B than of BD in this sample. The statistical details are given in Table 2 and explained in Figure 1.

Clinical symptoms and personality traits

The diagnostic group of BD + PD-B comorbidity exhibited the largest differences in clinical symptoms and personality traits. Subjects with comorbidity had a larger number of hospitalizations (z=-2.755, p=0.016) and self-injuries (a trend, z=-2.177, p=0.623) compared with patients diagnosed with PD-B alone. They also had more suicide attempts (trend, z=-2.348, p=0.07), hospitalizations (z= -2.564, p=0.027) and self-injuries (z=3.012, p=0.009) than patients with DM. The age of the patient at the onset of clinical symptoms was significantly younger in the group with comorbidity than in the group with BD alone (z =-2.271, p=0.021) and MD (z=2.756, p=0.005). Finally, the comorbidity group, compared with the BD group, exhibited more schizoid, schizotypal, antisocial, narcissistic and borderline personality traits (all $p \leq 0.05$).

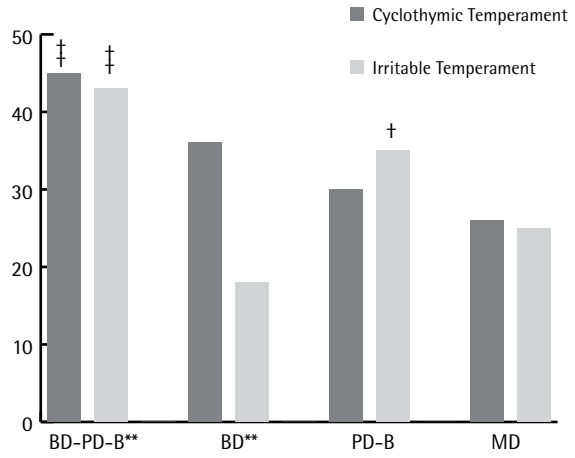
CONCLUSIONS

Although the multiaxial classification of DSM-IV allows the joint diagnosis of personality disorders and mood disorders, the internal and external validity of personality disorders has been questioned as independent of Axis I

Table 2 Differences in affective temperament between diagnostic groups

TEMPS	*Kruskal Wallis* x^2	Diagnostic Groups Range of mean			
		BD	MD	PD-B	BD + PD-B
Total	7.092	26.38	27.39	31.37	41.68 ǂ
Dysthymia	2.322	25.50	33.95	35.53	31.29
Cyclothymia	11.997**	27.38	25.95	28.60	45.03 ǂ
Hyperthymia	1.691	34.08	28.32	30.80	35.71
Irritable	16.342**	18.50	25.95	38.20 †	42.82 ǂ
Anxiety	0.731	39.17	32.32	30.08	34.71

x^2: Chi-square, BD: bipolar disorder, MD: major depression, PD-B: cluster B personality disorder
BD+PD-B: Bipolar disorder and cluster B personality disorder comorbidity.
* The difference is significant at p<0.05 / / ** The difference is significant at p<0.01.
† Comparison between groups with the Mann-Whitney U test:
Irritable Temperament, significant difference between PD-B and BD: p<0.05
ǂ Comparison between groups using the Mann-Whitney U test:
TEMPS total score, significant difference between BD+PD-B and all other groups: p<0.05.
Cyclothymic Temperament; significant difference between BD + PD-B and all other groups: p<0.05.
Irritable Temperament; significant differences between BD+PD-B and BD: p<0.01 and MD: p<0.01, respectively.



Cyclothymic temperament (according to TEMPS) was greater in patients with comorbidity than in the other diagnostic groups (PD-B, BD and MD), indicating that this temperament is more marked when BD and PD-B present together (z=-2.444, p=0.015). Furthermore, irritable temperament shown to be more frequent in patients with comorbidity and with PD-B alone, compared to patients who have BD and MD (z=-2.900, p=0.003). This suggests that irritable temperament may be more typical of PD-B than of BD.

Figure 2 *Significant differences in affective temperament (TEMPS)*

disorders.[26] Beyond the current diagnostic classification, it is necessary to evaluate the elements of the two disorders that differentiate them or are similar. This approach would help to clarify doubts about the future taxonomy and facilitate pharmacologic and psychosocial treatment, as it targets specific behaviors and dimensions rather than general diagnoses.[25]

The aim of this study was to analyze patients with affective disorders (BD and major depression [MD]), cluster B personality disorders (PD-B) and comorbidity (BD+PD-B) with instruments that assess cognitive, affective and behavioral elements of mood and thus detect distinctive characteristics of the diagnostic groups. We proceeded by assessing the characteristics of the emotional temperament, personality traits, and symptoms of the bipolar spectrum and mood spectrum of patients, in addition to demographic and clinical characteristics. The subsequent aim was to identify differential markers in BD+PD-B comorbidity to contribute to advancing the differential diagnosis and clarification of the debate on the overlap between mood disorders and cluster B personality disorders.

Patients with bipolar disorder and cluster B personality disorder comorbidity (BD+PD-B), had a younger age at onset and more severe affective symptoms, suicide attempts, hospitalizations and self-inflicted harm behaviors. They exhibited significantly more cyclothymic and irritable temperament traits and group A and B personality traits than patients diagnosed with BD alone. The comorbidity group represents a more severe type of emotional dysregulation than the other groups in this sample, including BD and PD-B alone. Patients with PD-B obtained intermediate scores for manic symptoms, i.e., higher scores than patients with MD and lower scores than patients with BD. Despite

this, the bipolarity index clearly distinguished patients with BD or comorbidity from other diagnostic groups (PD-B and MD). Finally, patients with comorbidity had higher scores for cyclothymic temperament than other diagnostic groups, indicating that cyclothymic temperament is more marked when BD and PD-B occur together. Patients with comorbidity and patients with PD-B alone showed higher scores for irritable temperament compared to patients with BD or MD, suggesting that irritable temperament is more typical of PD-B than of BD.

DISCUSSION

The main limitations of this study were the small sample size and the use of self-administered instruments to assess mood symptoms and emotional temperament. However, none of these limitations invalidates the findings. Regarding this point, it is worth mentioning that both TEMPS-A[44] and MOODS-SR [35] have been validated and found to be reliable in their self-administered version. As for the small sample size, it was controlled using nonparametric tests and the results were found to coincide with those of other studies in terms of the severity and topography of the symptoms and clinical features of BD + PD-B comorbidity.[45,46] The lack of statistical significance of the score for manic symptoms between BD and PD-B (in the *mania* domain of MOODS-SR) could represent a type II statistical error. Despite that, the finding of a mania score for the PD-B group with an intermediate value between the scores of the BD and MD groups indicates a more prominent presence of symptoms in the hypomania/mania series in that group (PD-B) than in patients with major depressive disorder. This finding becomes more relevant when taking into account that, as has been reported, scores in the *mania* domain of MOODS (symptoms of the hypomania/mania series throughout life) increase in direct relation to the severity of the depressive symptoms of recurrent unipolar depression.[47]

We consider it fundamental to take into account both the differences found between diagnostic groups and those not found. In general terms, no significant differences were detected in the domain of *rhythmicity* and vegetative functions between bipolar, depressive and PD-B disorders. The domain of *rhythmicity* and vegetative functions of MOODS explores changes in energy level, physical well-being, and mental and physical efficiency related to weather and seasons, as well as changes in eating behavior, sleep and sexual activities.[34] Such changes in feelings of well-being, activity and vegetative functions, which are theoretically related to cyclothymic temperament, did not show the expected difference between the BD and/or PD-B groups compared with the MD group. Similarly, cyclothymic temperament assessed using TEMPS-A showed no significant differences in score between the BD and other groups without comorbidity, despite reports from other studies that cyclothymic temperament is characteristically predominant in BD, including relatives of patients with BD, compared with controls.[37,48] These results regarding intermediate scores for symptoms of hypomania/mania throughout life in patients with PD-B, and the lack of significant differences in scores for cyclothymic, dysthymic and hyperthymic temperaments in this sample of patients with mood disorders and cluster B personality disorders could be arguments in favor of the spectrum theory of mood disorders,[45] as proposed by Kraepelin.[49] However, the BI distinguished patients with BD from those who did not have BD according to the MINI, including those with BD not otherwise specified, with excellent sensitivity and very good specificity. It remains to be determined which items supported this differentiation.

The results of the study revealed clear differences between subjects with BD+PD-B comorbidity and the other diagnostic groups. The significance of these differences is summarized in three concluding observations on the final considerations. Specific findings were highlighted for borderline PD, as the predominant PD-B, in the conclusions and introduction of the study for two main reasons. First, changes in the taxonomy of PD proposed for the next edition of the DSM (V), and recently approved, unify the nosological entities of PD-B into the same diagnosis, called "borderline type personality disorders." Second, borderline PD has received special attention in the field of clinical research in the past three decades, being the PD most studied in comorbidity with mood disorders. In view of the above considerations, emphasis has been given to research findings about borderline PD without overlooking the main contributions of the study of TP-B in general. Thus, the findings of the current investigation may be useful for research undertaken with the current classification of TP-B as well as the upcoming DSM-5.

Comorbidity as an indicator of clinical severity

It is likely that comorbidity might explain much of the heterogeneity in the evolution, functioning and response to treatment in BD.

Several studies have shown that patients with BD+PD-B comorbidity present more affective lability, impulsivity, anxiety, depression and hostility, more affective temperament traits, younger age at onset and, even, less response to treatment.[45,46,50,51] It has also been reported that in comorbidity with borderline PD in particular, BD shows significantly more cyclothymic temperament traits, rapid cycling and mixed states.[52,53] Borderline PD presents greater mood lability in comorbidity compared to each disorder separately.[54,55] In addition, characteristic factors have been identified in BD + borderline PD, such as substance abuse, history of trauma and attention deficit hyperactivity

disorder (ADHD) in childhood, and higher rate of leaving both psychotherapeutic and pharmacological treatment, compared to patients diagnosed with BD or borderline PD alone. Increased risk of suicide is one of the most serious aspects of comorbidity, which has important prognostic implications. Vieta et al.[56] compared 20 patients with BD II + borderline PD comorbidity to 20 patients with BD II alone. They found that more patients with comorbidity had suicide attempts (45%, p=0.003) or suicidal ideation (74%, p=0.003) than patients without comorbidity. This suggests that the risk of suicide is even higher in patients with BD and borderline PD than the already high risk associated with BD.

Comorbidity as a stage of progression

Berk et al.[57] have suggested that comorbidity is an indicator of the stage of progression of BD. This is supported by the stage model proposed by several authors, which consists in rating the severity of BD by stages. Some researchers suggest that comorbidity in adults is an advanced stage of bipolar type disorder that manifests itself at inception as borderline PD. However, others consider it a complex, polymorphic phenotypic manifestation of both disorders simultaneously.[50] The stage model proposes that clinical variables be evaluated longitudinally to assess comorbidity, functioning, neurocognition and interepisodic biomarkers as stages in the progression of the disorder. Kapczinski et al.[58] presented a clinical model of BD stages associated with the degree of functional impairment, presence of biomarkers and severity of the picture in the longitudinal evaluation. In short, understanding comorbidity as a stage in the progression of the pathological picture makes it easier to understand the underlying mechanisms, know the progression and plan treatment.

Systematic assessment of comorbidity

The controversy about the meaning of comorbidity remains unresolved. It is not yet possible to determine whether comorbidity is actually two independent biological conditions, a background risk marker, bipolar disorder subtype or simply a set of symptoms that overlap due to taxonomic imperfection.

In this study, we included all the cluster B personality disorders in addition to borderline PD in the analysis, as they are known to overlap with each other. The overlap is so important that in the taxonomy of DSM-5, PD-B will be unified as "borderline type" PD (except antisocial),[4] as mentioned above.

Our aim was to identify the differential elements between diagnoses that are controversial and we included comorbidity as a separate entity. The findings of the study show that not only are there certain elements that differentiate BD and PD-B, but that both disorders are altered in specific ways in comorbidity. Further study of comorbidity is necessary. Evaluating comorbidity has been useful in different ways. It has proven useful in differentiating between unipolar depression and bipolar depression, revealing that the presence of borderline PD traits in a depressive episode may be an indication that the depression is bipolar.[59,60] It is important to evaluate Axis II in the presence of bipolar disorders because the presence of Axis II conditions adversely affects the course of BD in terms of time to recovery, the severity of residual symptoms, number of medications prescribed and substance abuse.[54] In summary, in view of previous research and the findings of the present study we suggest that emotional temperament, personality traits, age at onset, frequency and severity of self-inflicted harm and suicide attempts, and admissions should be evaluated. This may facilitate the diagnosis and improve the effectiveness of the treatment (pharmacological and psychotherapeutic) of BD, PD-B and comorbid conditions, in addition to optimizing the differential diagnosis, detection of the stage of progression of the disorder and scientific study of the disorders in question.

Regardless of whether PD-B should be classified or not as a variant of BD, when the two present as comorbid conditions they show distinctive features with respect to how they manifest separately. Therefore, to detect the comorbidity that occurs so frequently, it often is necessary to maintain the identity of the PD-B as a separate entity from the mood spectrum disorders and to maintain the identity of bipolar disorders. Thus, comorbidity can be sought out as an independent entity for its correct diagnosis and effective treatment. Considering comorbidity as a clinical entity or subgroup of the mood disorders may help resolve the debate about BD and borderline PD, in particular and about BD and PD-B in general.

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