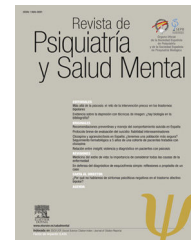




Revista de Psiquiatría y Salud Mental

www.elsevier.es/saludmental



REVIEW ARTICLE

Epidemiological and clinical variables related with the predominant polarity on bipolar disorder: A systematic review[☆]



Jesús García-Jiménez^a, Marisol Álvarez-Fernández^b, Lidia Aguado-Bailón^c,
Luis Gutiérrez-Rojas^{d,*}

^a Centro de Rehabilitación Psicosocial San Juan de Dios, Teruel, Spain

^b Unidad de Hospitalización de Salud Mental, Hospital Obispo Polanco, Teruel, Spain

^c Unidad de Hospitalización de Salud Mental, Hospital de Poniente, El Ejido, Almería, Spain

^d Unidad de Hospitalización, Hospital Campus de la Salud, Complejo Hospitalario de Granada, Granada, Spain

Received 13 January 2017; accepted 14 June 2017

Available online 2 March 2019

KEYWORDS

Bipolar disorder;
Predominant polarity;
Manic;
Depressive

Abstract

Introduction: Current classification of bipolar disorder (BD) in type I or type II, however useful, may be insufficient to provide relevant clinical information in some patients. As a result, complementary classifications are being proposed, like the predominant polarity (PP) based, which is defined as a clear tendency in the patient to present relapses in the manic or depressive poles.

Methods: We carried out a search in PubMed and Web of Science databases, following the Preferred Items for Reporting of Systematic Reviews and Meta-Analyses – PRISMA – guidelines, to identify studies about BD reporting PP. The search is updated to June 2016.

Results: Initial search revealed 907 articles, of which 16 met inclusion criteria. Manic PP was found to be associated with manic onset, drug consumption prior to onset and a better response to atypical antipsychotics and mood stabilisers. Depressive PP showed an association with depressive onset, more relapses, prolonged acute episodes, a greater suicide risk and a later diagnosis of BD. Depressive PP was also associated with anxiety disorders, mixed symptoms, melancholic symptoms and a wider use of quetiapine and lamotrigine.

Limitations: Few prospective studies. Variability in some results.

[☆] Please cite this article as: García-Jiménez J, Álvarez-Fernández M, Aguado-Bailón L, Gutiérrez-Rojas L. Factores asociados a la polaridad predominante en el trastorno bipolar: una revisión sistemática. Rev Psiquiatr Salud Ment (Barc). 2019;12:52–62.

* Corresponding author.

E-mail address: gutierrezrojas@hotmail.com (L. Gutiérrez-Rojas).

PALABRAS CLAVE

Trastorno bipolar;
Polaridad
predominante;
Maníaco;
Depresivo

Conclusion: PP may be useful as a supplement to current BD classifications. We have found consistent data on a great number of studies, but there is also contradictory information regarding PP. Further studies are needed, ideally of a prospective design and with a unified methodology. © 2017 SEP y SEPB. Published by Elsevier España, S.L.U. All rights reserved.

Factores asociados a la polaridad predominante en el trastorno bipolar: una revisión sistemática
Resumen

Introducción: Las actuales clasificaciones del trastorno bipolar (TB) en tipo I y tipo II, aunque han demostrado utilidad, aportan una información clínica insuficiente en algunos pacientes. Por ese motivo se han propuesto clasificaciones complementarias como la basada en la polaridad predominante (PP) que es definida como la tendencia clara a que el paciente presente recaídas de polaridad maniaca o depresiva.

Métodos: Revisión en los buscadores PubMed y Web of Science según las recomendaciones de la Preferred Items for Reporting of Systematic Reviews and Meta-Analyses-PRISMA-de todos los artículos sobre el TB en los que se analizara la PP, actualizada a junio de 2016.

Resultados: La búsqueda inicial mostró 907 artículos, de los cuales 16 cumplieron criterios de inclusión. La PP maniaca se asoció a las formas de inicio maníacas, al consumo de tóxicos anterior al TB y a una mejor respuesta a antipsicóticos atípicos y a eutimizantes. La PP depresiva se relacionó con comienzos depresivos, más recaídas, episodios agudos prolongados, mayor riesgo suicida y con un mayor retraso hasta el diagnóstico de TB. También con los trastornos de ansiedad, los síntomas mixtos y melancólicos y el uso de lamotrigina y quetiapina.

Limitaciones: Variabilidad en los resultados. Pocos estudios prospectivos.

Conclusión: La PP puede resultar de utilidad como complemento a las actuales clasificaciones del TB. Se dispone de datos consistentes en numerosos estudios, pero existen otros contradictorios. Se necesitan más estudios prospectivos y con una metodología unificada.

© 2017 SEP y SEPB. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Introduction

Bipolar disorder (BD) is a chronic mood disease which affects 2.4% of the population worldwide.^{1,2} The standard course of the disease is depressive episodes alternating with other (hypo) manic and mixed states.³

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5, BD is divided into BD type I (BDI), which is characterised by the presence of manic episodes throughout the course of the disease and BD type II (BDII), the diagnosis of which requires at least one depressive and another hypomanic episode.⁴ For its part, the tenth review of the International Classification of Diseases (ICD-10)⁵ distinguishes a first large group generically called "bipolar disorder", in which the nature of the current episode (manic, hypomanic or depressive) determines its classification and a second group called "other bipolar disorders" which includes BDII. Although these classifications provide useful information, additional encoders have been proposed, which support the clinical symptoms in addressing this complex disease.

Classification based on predominant polarity (PP) were formulated by Angst in 1978, after having conducted a 16 year old follow-up of a sample of 95 bipolar patients.⁶ He

observed that although several patients had not demonstrated a clear tendency and relapsed in both manic and depressive episodes (which he called "nuclear" type), others typically decompensated towards the depressive pole ("predominantly depressive") and the remainder towards the manic pole ("predominantly manic"). Belonging to one group or another had major repercussions on practice, as each one presented with different sociodemographic, clinical, prognostic characteristics or response to treatments.

Nowadays there is renewed interest in this type of encoding,⁷⁻⁹ and it has been estimated that up to 50% of patients may be classed according to the PP.^{7,10} However, at present there are no common criteria used by psychiatrists for this, the most highly used being those proposed by Colom et al. (Barcelona proposal).¹¹ According to these authors, if at least two thirds of relapses were depressive, then polarity would be predominantly depressive (PDP), whilst if two thirds of relapses were manic, then polarity would be predominantly manic (PMP).

The lack of common criteria for use may explain the existence of contradictory data in the literature, so that PP was not included as a complimentary encoder in current manuals of classification of psychiatric diseases despite its potential usefulness in clinical practice, as has been shown in multiple studies.

For this reason, we conducted a bibliographic search in the main data bases to identify variables of interest in BD which are related to PP. We think this information will provide relevant data for the research and challenge of this complicated disease.

Methods

For this study we followed the international recommendations of the preferred items for Reporting of Systematic Reviews and Meta-Analyses – PRISMA-.¹² The data bases used were the Web of Science and Pub Med, with a deadline date of inclusion for articles of 1st June 2016.

The search parameters in PubMed were (“bipolar disorder”[MeSHTerms] OR («bipolar»[AllFields] AND «disorder»[AllFields]) OR «bipolar disorder»[AllFields] OR («bipolar»[AllFields] AND «disorders»[AllFields]) OR «bipolar disorders»[AllFields] AND «polarity»[AllFields] OR (predominant[AllFields] AND polarity[AllFields]), whilst in the Web of Science they were bipolar disorder AND polarity OR predominant polarity.

Inclusion criteria were established as articles in English or Spanish on patients diagnosed with BD according to the International Classification of Diseases, 10th review, or the DSM (DSM-III-R to DSM-5) where PP was analysed. In them, the definition of which polarity is used should be clear and 70 was the minimum number of participants established (on considering this figure to be appropriate to detect significant differences among the groups after reading previous related studies).¹³ Experimental type articles were excluded, those which did not treat l BD or PP, and studies which presented a lower sample size than that indicated. The main researcher (JGJ) was in charge of initial screening, through the reading of titles and abstracts.

Results

Initial search showed up 907 studies, of which 875 were excluded for not treating BD or PP. Out of the remaining 32, only 16 met with inclusion criteria (Fig. 1). The variables of interest analysed were: (a) definition of predominant polarity; (b) rates of prevalence; (c) associated socio-demographic variables; (d) clinical variables and (e) implications in clinical management. Results are summarised in Table 1.

Definition of predominant polarity

In 11 of the 16 selected articles, the definition of the PP used was the Barcelona proposal, based on the two thirds criteria.¹¹ This criteria establishes an arbitrary cut-off point from which a person presented a PMP when two thirds of their relapses were manic or PDP if they were depressive. Posterior authors followed this definition.^{10,14–18}

Three studies simplified the cut-off point displacing it up to 50%,^{9,19,20} whilst the remaining 2 established the PP in accordance with the most frequent recurrence in absolute terms.^{21,22}

All these criteria were compared in a multicentre study which concluded that less restrictive definitions would allow

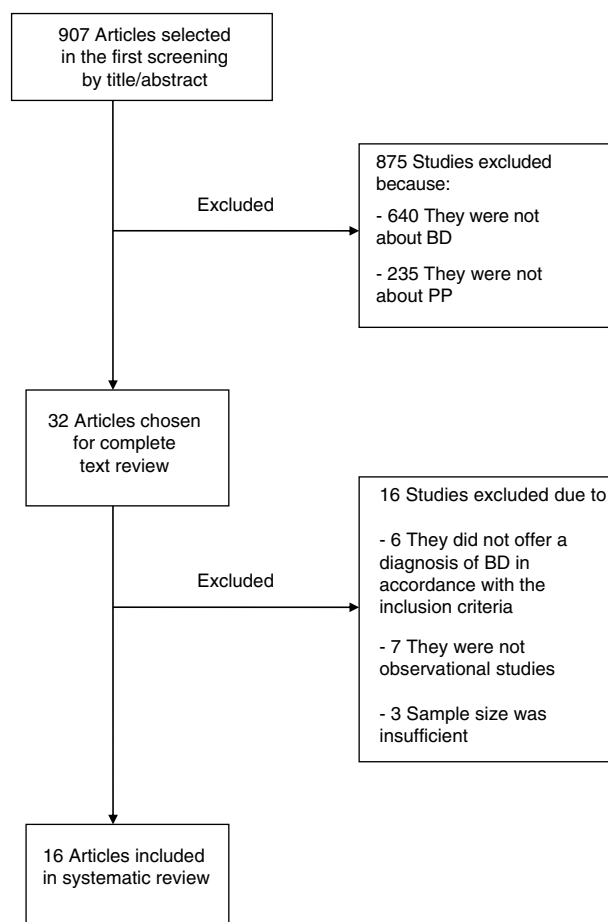


Figure 1 Article selection process.

more patients to be coded according to PP, but without this being associated with significant differences between the groups.⁷

Prevalence

In the reviewed studies, the prevalence of patients for whom a polarity could be identified ranged between 42.4% and 71.8% (median of 52.7%). For PMP this value was 12.4%–55.0% (median of 26%) and in the case of PDP it was 17.0%–34.1% (median of 21.4%). Studies with large samples^{14,23,24} and with more patients diagnosed with BDII^{10,11,24,25} presented higher rates of PDP, whilst the PMP was mostly associated with the BDI.^{7,9,15,17}

Socio-demographic variables

Articles which did not analyse the PP indicate that mania is more common in men^{26,27} and depression in women,^{28,29} but when polarity is studied this statement does not appear to be as clear. If PPM is associated with the male²⁴ and PDP with the female^{7,16} in some articles, there are authors who did not find any gender differences.^{7,9,11,15,18,20}

Disparity also exist with regards to a family history of BD, since one study showed a higher family load in PDP²² and

Table 1 Summary of the main characteristics of the articles on predominant polarity in bipolar disorder included in the review.

Authors and year	Country	Sample	Type of study	PP definition	Conclusions
Henry et al. ²¹ (1999)	France	72 BDI patients DSM-IV criteria	Cross-sectional	Simple percentage of manic and depressive episodes	Manic episodes related negatively with depressive temperament
Daban et al. ²⁹ (2006)	Spain	300 BDI and BDII patients DSM-III-R criteria	Cross-sectional	Greater number of episodes of one polarity than the other	The onset of a depressive episode are related to PDP
Colom et al. ¹¹ (2006)	Spain	224 BDI and BDII patients DSM-III-R criteria	Cross-sectional	More than two thirds of the episodes of a specific polarity throughout life	PDP is the most frequent in this sample <i>Variables associated with PDP:</i> BDII, onset of depressive episode, stressful life events and substance abuse prior to first episode, seasonal and melancholic pattern, suicide attempts and mixed episodes. Higher use of lamotrigine, antidepressants and antipsychotics in maintenance <i>Variables associated with PMP:</i> early onset of disease, higher number of manic episodes (but not hypomanic), more hospital admissions and greater use of antipsychotics in acute phase PMP more frequent in this sample
Osher et al. ⁹ (2000)	Israel	71 BDI patients DSM-IV criteria	Retrospective	Over 50% of episodes of a specific polarity throughout life	
Goikolea et al. ²⁴ (2007)	Spain	325 BD patients DSM-IV criteria and seasonal pattern	Prospective 10 year follow-up	Over two thirds of episodes of a specific polarity throughout life	Seasonal pattern associated with PDP and BDII. Posterior multivariate analysis: only the association with BDII persisted
Rosa et al. ¹⁰ (2008)	Brazil	149 BD patients DSM-IV-TR criteria	Cross-sectional	Over two thirds of episodes of a specific polarity throughout life	<i>Variables associated with PDP:</i> greater delay in diagnosis, forms of depressive onset and BDII. Also higher number of suicide attempts and greater duration of disease.
Forty et al. ¹⁹ (2009)	United Kingdom	552 BD I patients CIE-10 and DSM-IV criteria	Cross-sectional	Over 50% of episodes of a specific polarity throughout life	<i>Variables associated with PDP:</i> related to forms of depressive onset <i>Variables associated with PMP:</i> related to manic forms of onset
García-López et al. ¹⁴ (2009)	Spain	296 BD patients DSM-IV-TR criteria	Prospective 1–4 years follow-up	Over two thirds of episodes of a specific polarity throughout life	46% of PP in the sample, 24% of PDP and 22% of PMP. In follow-up no relationships were established with sub threshold symptoms
Mazzarini et al. ¹⁵ (2009)	Italy	124 BDI patients and 19 unipolar depression patients DSM-IV criteria	Cross-sectional	Over two thirds of episodes of a specific polarity throughout life	Higher prevalence of PMP in their sample <i>Variables associated with PDP:</i> higher plans for suicide and forms of depressive onset No differences between PDP and PMP in emotional temperament

Table 1 (Continued)

Authors and year	Country	Sample	Type of study	PP definition	Conclusions
Vieta et al. ¹⁸ (2009)	Multicentreo	833 BDI patients and 788 patients with baseline information and follow-up DSM-IV criteria	Multicentre randomised clinical trial (olanzapine vs. olanzapine plus fluoxetine vs. placebo)	Over two thirds of episodes of a specific polarity throughout life	Higher rates of PDP in this sample <i>Variables associated with PDP:</i> higher frequency of psychotic symptoms <i>Variables associated with PMP:</i> rapid cycling in males. Greater response to treatment in depressive phase
González-Pinto et al. ²⁰ (2010)	Spain	169 BDI patients DSM-IV criteria	Prospective	Over 50% of episodes of a specific polarity throughout life	PDP most frequent in this sample <i>Baseline:</i> PMP with lower onset ages and higher number of hospital admissions. PDP with more suicide attempts, family history of emotional symptoms and married civil status. No differences between both groups in substance abuse. After 10 years of follow-up: PDP more relapses, more suicide attempts and more hospital admissions. Lower consumption of alcohol and other drugs in the PMP group
Nivoli et al. ¹⁶ (2011)	Spain	604 BD patients DSM-IV-TR criteria	Cross-sectional	Over two thirds of episodes of a specific polarity throughout life	PDP most frequent in their sample Association between female gender and PDP
Baldessarini et al. ⁷ (2012)	Multicentre	928 BDI patients	Cross-sectional	Over two thirds of episodes of a specific polarity throughout life	PMP more common in their sample <i>Variables associated with PDP:</i> delay in diagnosis of BD, first depressive or mixed episode, suicide attempts and married civil status <i>Variables associated with PMP:</i> first manic or psychotic episode, ≥12 years of academic training, family history of emotional disorders <i>Multivariate analysis:</i> the intention to commit suicide remained and there was delay in diagnosis associated with PDP <i>Suicide risk:</i> data provided by USA and Spain on mixed symptoms. If the mixed episodes are combined with depressive episodes, the risk of suicide is doubled.
Nivoli et al. ²² (2013)	Spain	604 BD (I, II and NOS category) patients DSM-IV criteria	Observational	Over two thirds of episodes of a specific polarity throughout life	<i>Variables associated with PDP:</i> associated with so-called "group of antidepressants and stabilisers" <i>Variables associated with PP:</i> associated with so-called "antimanic drugs"

Table 1 (Continued)

Authors and year	Country	Sample	Type of study	PP definition	Conclusions
Pacchiarotti et al. ¹⁷ (2013)	Italy	187 BDI patients DSM-IV criteria	Cross-sectional	Over two thirds of episodes of a specific polarity throughout life	Mixed symptoms (anxiety, motor tension, risk of suicide, motor hyperactivity and excitability) associated with PDP. Subsequent multivariate analysis did not show up this association
Popovic et al. ²³ (2013)	Spain	604 BDI patients and II, 257 classified under PP DSM-IV-TR criteria	Observational	Over two thirds of episodes of a specific polarity throughout life	PDP more frequently in this sample <i>Variables associated with PDP:</i> BDII, forms of depressive onset, stressful life events prior to onset, melancholic symptoms and high rates of suicide attempts Higher use of lamotrigine, benzodiazepine and antidepressants <i>Variables associated with PMP:</i> male, Young, BDI, substance abuse prior to disease, early disease onset, high hospitalisation rates and early age, more psychotic symptoms (at onset and throughout the course of the disease) Higher usage of olanzapine, risperidone and neuroleptics

SNRI: selective noadrenalin reuptake inhibitors; SSRIs: selective serotonin reuptake inhibitors; NOS: bipolar disorder not otherwise specified; PP: predominant polarity; PDP: predominant depressive polarity; PMP: predominant manic polarity; BD: bipolar disorder.

the other in PMP,⁷ whilst in a different article no relevant differences were found.¹⁵

For its part, the association between a high academic level and PMP appears clearer, and also that patients with PDP are usually married or live more frequently with their partners.⁷

Clinical variables

Age at onset and polarity of the first episode

Population studies indicate that the mean age of starting with BD is between 17 and 27 years,³⁰ whilst diagnosis of a first manic episode usually occurs earlier, between 15 and 18 years of age.²² Compared with other emotional disorders, the start of BD is early,³¹ often in the form of a depressive episode (up to 67% at onset).^{22,32}

As occurred with gender, this reality appears more complex when polarity is considered, since although several studies showed that onset of PMP came before that of PDP (24.77 vs. 30.69 years),^{20,22} other articles show early onset of PDP (24 ± 1.97 vs. 29 ± 11 years),¹⁰ and similarly there are authors who did not find any significant differences between both polarities (mean age of onset as 22 years).^{7,11}

However, there is consensus regarding the type of symptoms of the first episode and posterior PP, since the beginning of manic episodes are associated long term with PMP^{7,19,24} and the start of depressive and mixed symptoms will more probably develop into a PDP in the future.^{7,10,19,24}

Number of relapses and duration of the acute episode. The imbalances in BD are a key prognostic factor, as they lead to progressive impairment in the functional areas of the patient, increasing treatment resistance.²⁴ In BD depressive relapses are usually briefer than unipolar depression, particularly for PMP,¹⁵ in which mean duration of an episode is of 2.5 months compared with 2.86 months of PDP and 5.7 months of unipolar depression.¹⁵ Furthermore, the majority of studies have shown that in PDP, both the number of relapses (of any type) and their duration is higher than in manic polarity.^{7,10,20,22} However, not all studies coincide, as several have shown an annual mean recurrence rate which is similar for both PP.⁷

Relationship with suicide and substance abuse. BD entails great suffering for the person, with suicide rates of up to 10%–15% in long-term follow-up.¹⁰ Figures governing suicide attempts and suicides are higher in PDP.^{7,11,20,24} with figures doubling if patients with mixed symptoms are taken into account.^{7,11}

Many publications have shown that substance abuse in BD is up to 27% more common than in the general population,³³ with alcohol and cannabis being the substances most highly consumed, followed by cocaine and opioids.³⁴ Alcohol abuse is most associated with depressive symptoms both at initial stages and in subsequent relapses,³⁵ whilst cannabis is related to manic imbalances and more severe acute episodes.^{11,36}

In our review the articles which used a more restrictive definition of polarity showed that substance abuse is higher in PMP,^{7,10} but PDP had more lax definitions and presented with higher rates.⁷ Moreover, substance abuse appears to precede the onset of BD more frequently in PMP than in PDP.^{11,22,24}

Comorbidity. The prevalence of comorbidity in BD with other psychiatric disorders is very high, particularly in disorders of anxiety, personality and substance abuse. Regarding polarity, PDP has higher rates of co morbidity^{18,22} (especially with anxiety disorders),¹⁰ although one of the selected articles did not find any significant differences between both polarities.⁷

Regarding organic disorders, CNS injuries, aids and head injuries have been typically associated with BD. Only in one of the studies selected was this issue analysed, but without provision of any conclusive data.¹¹

Other clinical variables clinics analysed. In BD diagnosis is often delayed between 4 and 10 years since the onset of symptoms. This is much more apparent in PDP, since in these patients the first manic episode may take place after several prior depressive relapses.^{7,10} Also, patients with depressive polarity are usually more oftener diagnosed with BDII^{8,10,11,24,25} and present on more occasions with melancholic symptoms (psychomotor delay and catatonia).^{11,24}

Most of the selected studies,^{8,20,24} but not all,¹⁵ showed that the frequency of hospital admissions is greater in patients with manic polarity and this is associated with a worse long-term prognosis. In PMP psychotic symptoms are also more frequent in the first episode^{7,24} and in the disease evolution,²² with their presence being associated more with more serious and prolonged relapses to higher hospitalisation rates. In contrast, other authors found there was a higher prevalence of psychotic symptoms in PDP.^{16,18}

One study linked PMP with rapid cycling (defined as 4 episodes or more in the same year)¹⁸ and in another a seasonal pattern was found in patients with depressive polarity,¹¹ although the latter could not be later replicated.²⁴

At present the role of the so-called emotional temperaments is being analysed, i.e. those lower forms mood variation, relatively stable throughout life, which according to some authors correspond with sub-syndromic manifestations of major emotional disorders.³⁷ Five types have been described (hyperthymic, cyclothymic, depressive, irritable and anxious temperament), the combined prevalence of which has been described in population studies as 20%.³⁷ There is also a strong biological correlation related to changes in serotonin and dopamine,³⁷ and whilst the depressive temperament is observed more in the PDP, the hyperthymic temperament is typical of manic polarity.³⁷ However, a recent publication also related PMP with the cyclothymic temperament.³⁸

To finalise this section we will briefly summarise 2 important issues in BD, which are the level of functionality and cognitive impairment. Recent studies have reported serious limitations in these patients in both social skills and in satisfactory interpersonal relationships.³⁹ These difficulties are associated with both a worse awareness of the disease, more prolonged depressive episodes, poorer general physical health⁴⁰ and higher rates of unemployment.⁴¹ Although the majority of the articles did not find any significant differences with regard to the functionality of the 2 types of polarity,^{10,20,22} one study showed a major dysfunction of the social type in PDP,¹¹ in keeping with other authors for whom depressive polarity implies worse autonomy, probably from a multifactorial origin where the worst response to treatments conditions a higher number of relapses.¹⁸

Similar to functionality, there is a growing interest in cognitive impairment observed in patients with BD, since it appears that these changes occur both in relapses and in phases of euthymia, and although they may be of lower intensity than that of schizophrenia, functions deteriorate such as the ability to pay attention or the working memory, among others.⁴² It seems clear that impairment worsens with successive relapses,⁴³ but no specific studies in PP are available.

Treatment implications

Response to treatment for BD is multifactorial, and is impacted by variables such as previous relapses of the patient, their level of therapeutic adherence, associated comorbidity and substance usage.²⁴

Polarity also appears to be important, as one study showed that patients with PMP responded better than patients with PDP to the combination of fluoxetine + olanzapine for the treatment of depressive episodes.¹⁸

One of the studies also analysed general prescription data, showing that in PMP the use of the so-called "combined antimanic" drug was more frequent, which are mood stabilisers (lithium, valproic acid, and carbamazepine) and atypical antipsychotics (clozapine, risperidone and olanzapine). However, lamotrigine and quetiapine are prescribed more in PDP and the use of antidepressants is reduced to a small group of patients with BDII and depressive polarity.²³ However, there was an article which did not find any differences in the use of mood stabilisers according to polarity type.⁷

At this point it is worthwhile highlighting the concept of the polarity index (PI) described by Popovic et al.²⁴ The PI is a numerical value given to each drug and which is the result of the ratio between its number required to treat to prevent a depressive episode and its number required to treat to prevent a manic episode. PI values above 1 indicate that this drug is of greater use as an antimanic agent (the atypical antipsychotics for example, and particularly risperidone, aripiprazole and olanzapine), and if the PI value is below 1, then the product is more effective as an antidepressant (lamotrigine). Drugs whose PI value is closer to 1 would have an antimanic power and similar antidepressant power (lithium and quetiapine).²⁴ The study by Popovic et al. Also shows that patients with PMP frequently receive treatment combinations where the PI combined is higher than in patients with PDP, which would indicate a greater antimanic effect in the first group, and this finding was repeated in a different sample.⁴⁴ Notwithstanding, other authors have doubted the use of the PI, on showing that it is complicated that a single statistical parameter may summarise the enormous variability in response to treatment in disorders as complex as BD.⁴⁵

Discussion

At present, not all patients with BD may be classified according to PP, with figures which range between 42.4% and 71.8% in reviewed studies. This may be due to the fact that in certain patients one polarity does not prevail over the other

("nuclear type" patients according to Angst), but it also may be due to the lack of unified criteria amongst the scientific community to define PP, as was shown in a recent publication.⁴⁶

The so-called "Barcelona proposal" (two thirds criteria) is more specific, and the precision in detecting a real case of PP therefore increases, but at the same time it may be over restrictive, since in several studies where it has been used, it was only possible to classify 56% of patients according to the PP.⁴⁶ In contrast, looser definitions increase the number of classifiable patients depending on their polarity, but at the risk of this classification being unstable over time and therefore largely irrelevant.⁷

Some studies have shown there is a higher ratio of PMP with the male, with high educational levels and with BDI, whilst PDP appears to be more associated with females, with being married and with BDII. However, the information provided by long-term follow-up studies^{47,48} have not been able to replicate these findings, which may be due to the presence of bias in studies included in this review.

The references deliver more consistent data on clinical variables. For example, the onset of depressive symptoms, the most common and prolonged relapses and comorbidity with anxiety disorders or a higher suicide risk are associated with PDP, where a greater delay in diagnosis is also observed. Mixed and melancholic presentations and the use of lamotrigine and quetiapine are also typical of this.

In contrast, the onset of mixed type, a background of the consumption of toxic substances prior to the onset of disease and a better response to atypical antipsychotics and mood stabilisers are characteristic of PMP.

Other factors such as the presence of a family history, long-term abuse of toxic substances, hospital stays, psychotic symptoms, rapid cycling, seasonal patterns, emotional temperaments and level of functionality, show varied information on their relationship with PP (Table 2).

All these data are in keeping with the results of a recent systematic review¹³ and demonstrate new lines of research and intervention, among which we would highlight excessive autolysis intent, for its impact in the mortality of patients with BD,⁴⁹ and especially in those with PDP. Another interesting strategy would be to raise awareness and reduce the consumption of toxic substances in teenagers and young adults due to their long-term association with PMP.¹³

Although throughout this study we have shown that polarity may be useful as a complement to the current BD classifications, factors such as the absence of a common definition or the lack of objective biological markers have impacted the fact that PP has not been included as an additional encoder in the DSM-5.⁴⁶ However, a recent meta-analysis has shown that together with the polarity of the first decomposition, analysis of the PP is of great help when selecting an effective treatment to prevent a future relapse.⁵⁰ According to this study, the risk of a further decompensation is maximum immediately after an episode (hazard ratio 1.89–5.14), particularly during the first year (44% of probability of experience a new relapse of the same polarity during that time).⁵⁰

Table 2 Summary of available evidence: conclusive and contradictory data.

Replicated data	<i>Depressive polarity</i>	Forms of depressive onset High number of relapses Prolonged acute episodes Suicidal behaviour Comorbidity with anxiety disorder Delayed diagnosis Mixed and melancholic forms of presentation More frequent use of quetiapine and lamotrigine
	<i>Manic polarity</i>	Forms of manic onset Background of consumption of toxic substances prior to disease onset Faster and better response to atypical antipsychotics and mood stabilisers
Contradictory data	<i>Demographical</i>	Male and high academic level with PMP Female and married with PDP
	<i>Clinical</i>	Link between BDI and PMP and between BDII and PDP Family history Long-term consumption of toxic substances Number of hospital admissions Psychotic symptoms Rapid cycling Seasonal pattern Temperament Psychosocial functionality

PDP: predominant depressive polarity; PMP: predominant manic polarity; BD: bipolar disorder.

Conclusions

The BD classifications described in the diagnostic manuals provide some information on the characteristics of this disease, and the use of additional encoders, such as PP, may help to complement this information. Throughout this study we have shown the statistically significant relationship of each polarity with different variables of interest in the approach to and treatment of BD, although the literature is not exempt from some contradictory data. This may be due to the absence of a common definition for analysing PP, but a great variety of methodology of the selected articles was also found. Further studies are needed for the future, essentially prospective studies and with a unified definition and methodology, so that reliability may be established for the relationship between PP and the relevant variables in BD patient follow-up.

Limitations

The main limitation of this study is the fact that it has not been possible to carry out a meta-analysis to provide a higher level of scientific evidence to the results, mainly due to the multiple variables analysed and to the heterogeneity in the methodology of the included articles.

Conflict of interests

The authors have no conflict of interests to declare.

References

1. Belmaker RH. Bipolar disorder. *N Engl J Med*. 2004;351:476–86.
2. Merikangas KR, Jin R, He JP, Kessler RC, Lee S, Sampson NA, et al. Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. *Arch Gen Psychiatry*. 2011;68:241–51.
3. Phillips ML, Kupfer DJ. Bipolar disorder diagnosis: challenges and future directions. *Lancet*. 2013;381:1663–71.
4. American Psychiatric Association. DSM-5. Manual diagnóstico y estadístico de los trastornos mentales. Editorial Médica Panamericana; 2014.
5. Organización Mundial de la Salud. CIE-10. Trastornos mentales y del comportamiento: descripciones clínicas y pautas para el diagnóstico. Madrid: Meditor; 1992.
6. Angst J. The course of affective disorders. *Arch Psychiatr Nervenkr* (1970). 1978;226:65–73.
7. Baldessarini RJ, Undurraga J, Vazquez GH, Tondo L, Salvatore P, Ha K, et al. Predominant recurrence polarity among 928 adult international bipolar I disorder patients. *Acta Psychiatr Scand*. 2012;125:293–302.
8. Colom F, Vieta E. The road to DSM-V. *Psychopathology*. 2009;42:209–18.
9. Osher Y, Yaroslavsky Y, el-Rom R, Belmaker RH. Predominant polarity of bipolar patients in Israel. *World J Biol Psychiatry*. 2000;1:187–9.
10. Rosa AR, Andreatza AC, Kunz M, Gomes F, Santin A, Sanchez-Moreno J, et al. Predominant polarity in bipolar disorder: diagnostic implications. *J Affect Disord*. 2008;107:45–51.
11. Colom F, Vieta E, Daban C, Pacchiarotti I, Sánchez-Moreno J. Clinical and therapeutic implications of predominant polarity in bipolar disorder. *J Affect Disord*. 2006;93:13–7.

12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg*. 2010;8:336–41.
13. Carvalho AF, McIntyre RS, Dimelis D, Gonda X, Berk M, Nunes-Neto PR, et al. Predominant polarity as a course specifier for bipolar disorder: a systematic review. *J Affect Disord*. 2014;163:56–64.
14. García-López A, de Dios-Perrino C, Ezquiaga E. Polarity of the first episode and predominant polarity in a cohort of bipolar outpatients. *Eur Neuropsychopharmacol*. 2009;19 Suppl. 3:S571.
15. Mazzarini L, Pacchiarotti I, Colom F, Sani G, Kotzalidis GD, Rosa AR, et al. Predominant polarity and temperament in bipolar and unipolar affective disorders. *J Affect Disord*. 2009;119:28–33.
16. Nivoli AM, Pacchiarotti I, Rosa AR, Popovic D, Murru A, Valenti M, et al. Gender differences in a cohort study of 604 bipolar patients: the role of predominant polarity. *J Affect Disord*. 2011;133:443–9.
17. Pacchiarotti I, Nivoli AM, Mazzarini L, Kotzalidis GD, Sani G, Koukopoulos A, et al. The symptom structure of bipolar acute episodes: in search for the mixing link. *J Affect Disord*. 2013;149:56–66.
18. Vieta E, Berk M, Wang W, Colom F, Tohen M, Baldessarini RJ. Predominant previous polarity as an outcome predictor in a controlled treatment trial for depression in bipolar I disorder patients. *J Affect Disord*. 2009;119:22–7.
19. Forty L, Jones L, Jones I, Smith DJ, Caesar S, Fraser C, et al. Polarity at illness onset in bipolar I disorder and clinical course of illness. *Bipolar Disord*. 2009;11:82–8.
20. González-Pinto A, Alberich S, Barbeito S, Alonso M, Vieta E, Martínez-Arán A, et al. Different profile of substance abuse in relation to predominant polarity in bipolar disorder. *J Affect Disord*. 2010;124:250–5.
21. Henry C, Lacoste J, Bellivier F, Verdoux H, Bourgeois ML, Leboyer M. Temperament in bipolar illness: impact on prognosis. *J Affect Disord*. 1999;56:103–8.
22. Daban C, Colom F, Sánchez-Moreno J, García-Amador M, Vieta E. Clinical correlates of first-episode polarity in bipolar disorder. *Compr Psychiatry*. 2006;47:433–7.
23. Nivoli AM, Colom F, Pacchiarotti I, Murru A, Scott J, Valenti M, et al. Treatment strategies according to clinical features in a naturalistic cohort study of bipolar patients: a principal component analysis of lifetime pharmacological and biophysical treatment options. *Eur Neuropsychopharmacol*. 2013;23:263–75.
24. Popovic D, Torrent C, Goikolea JM, Cruz N, Sánchez-Moreno J, González-Pinto A, et al. Clinical implications of predominant polarity and the polarity index in bipolar disorder: a naturalistic study. *Acta Psychiatr Scand*. 2013;129:366–74.
25. Goikolea JM, Colom F, Martínez-Arán A, Sánchez-Moreno J, Giordano A, Bulbena A, et al. Clinical and prognostic implications of seasonal pattern in bipolar disorder: a 10-year follow-up of 302 patients. *Psychol Med*. 2007;37:1595–9.
26. Robb JC, Young LT, Cooke RG, Joffe RT. Gender differences in patients with bipolar disorder influence outcome in the medical outcomes survey (SF-20) subscale scores. *J Affect Disord*. 1998;49:189–93.
27. Christensen EM, Gjerris A, Larsen JK, Bendtsen BB, Larsen BH, Rolff H, et al. Life events and onset of a new phase in bipolar affective disorder. *Bipolar Disord*. 2003;5:356–61.
28. Braunig P, Sarkar R, Effenberger S, Schoofs N, Kruger S. Gender differences in psychotic bipolar mania. *Gend Med*. 2009;6:356–61.
29. Altshuler LL, Kupka RW, Helleman G, Frye MA, Sugar CA, McElroy SL, et al. Gender and depressive symptoms in 711 patients with bipolar disorder evaluated prospectively in the Stanley Foundation bipolar treatment outcome network. *Am J Psychiatry*. 2010;167:708–15.
30. Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Arch Gen Psychiatry*. 2007;64:543–52.
31. Benazzi F, Berk M, Frye MA, Wang W, Barraco A, Tohen M. Olanzapine/fluoxetine combination for the treatment of mixed depression in bipolar I disorder: a post hoc analysis. *J Clin Psychiatry*. 2009;70:1424–31.
32. Perugi G, Micheli C, Akiskal HS, Madaro D, Socci C, Quilici C, et al. Polarity of the first episode, clinical characteristics, and course of manic depressive illness: a systematic retrospective investigation of 320 bipolar I patients. *Compr Psychiatry*. 2000;41:13–8.
33. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. *Arch Gen Psychiatry*. 1994;51:8–19.
34. Cerullo MA, Strakowski SM. The prevalence and significance of substance use disorders in bipolar type I and II disorder. *Subst Abuse Treat Prev Policy*. 2007;2:29.
35. Jaffee WB, Griffin ML, Gallop R, Meade CS, Graff F, Bender RE, et al. Depression precipitated by alcohol use in patients with co-occurring bipolar and substance use disorders. *J Clin Psychiatry*. 2009;70:171–6.
36. Baethge C, Baldessarini RJ, Khalsa HM, Hennen J, Salvatore P, Tohen M. Substance abuse in first-episode bipolar I disorder: indications for early intervention. *Am J Psychiatry*. 2005;162:1008–10.
37. Vázquez GH, Tondo L, Mazzarini L, Gonda X. Affective temperaments in general population: a review and combined analysis from national studies. *J Affect Disord*. 2012;139:18–22.
38. Azorin JM, Adida M, Belzeaux R. Predominant polarity in bipolar disorders: further evidence for the role of affective temperaments. *J Affect Disord*. 2015;182:57–63.
39. Cusi AM, Macqueen GM, McKinnon MC. Patients with bipolar disorder show impaired performance on complex tests of social cognition. *Psychiatry Res*. 2012;200:258–64.
40. Berk M, Berk L, Dodd S, Fitzgerald PB, de Castella AR, Filia S, et al. The sick role, illness cognitions and outcomes in bipolar disorder. *J Affect Disord*. 2013;146:146–9.
41. Wingo AP, Harvey PD, Baldessarini J. Neurocognitive impairment in bipolar disorder patients: functional implications. *Bipolar Disord*. 2009;11:113–25.
42. Henry C, M'Bailara K, Lépine JP, Lajnef M, Leboyer M. Defining bipolar mood states with quantitative measurement of inhibition/activation and emotional reactivity. *J Affect Disord*. 2010;127:300–4.
43. Hellvin T, Sundet K, Simonsen C, Aminoff SR, Lagerberg TV, Andreassen OA, et al. Neurocognitive functioning in patients recently diagnosed with bipolar disorder. *Bipolar Disord*. 2012;14:227–38.
44. Volkert J, Zierhut KC, Schiele MA, Wenzel M, Kopf J, Kittel-Schneider S, et al. Predominant polarity in bipolar disorder and validation of the polarity index in a German sample. *BMC Psychiatry*. 2014;14:322.
45. Alphas L, Berwaerts J, Turkoz I. Limited utility of number needed to treat and the polarity index for bipolar disorder to

- characterize treatment response. *Eur Neuropsychopharmacol.* 2013;23:1597–9.
46. Colom F, Vieta E, Suppes T. Predominant polarity in bipolar disorders: refining or redefining diagnosis? *Acta Psychiatr Scand.* 2015;132:324–6.
47. Judd LL, Akiskal HS, Schettler PJ, Coryell W, Endicott J, Maser JD, et al. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. *Arch Gen Psychiatry.* 2003;60:261–9.
48. Roy-Byrne P, Post RM, Uhde TW, Porcu T, Davis D. The longitudinal course of recurrent affective illness: life chart data from research patients at the NIMH. *Acta Psychiatr Scand Suppl.* 1985;317:1–34.
49. Angst J, Hengartner MP, Gamma A, von Zerssen D, Angst F. Mortality of 403 patients with mood disorders 48 to 52 years after their psychiatric hospitalization. *Eur Arch Psychiatry Clin Neurosci.* 2013;263:425–34.
50. Radua J, Grunze H, Amann BL. Meta-analysis of the risk of subsequent mood episodes in bipolar disorder. *Psychother Psychosom.* 2017;86:90–8.