



Predominant polarity in bipolar disorders: Further evidence for the role of affective temperaments

J.M. Azorin^{*}, M. Adida, R. Belzeaux

Department of Psychiatry, Sainte-Marguerite Hospital, 13274 Marseille Cedex 9 France

ARTICLE INFO

Article history:

Received 27 February 2015

Received in revised form

21 April 2015

Accepted 21 April 2015

Available online 29 April 2015

Keywords:

Bipolar disorder

Predominant polarity

Mania

Depression

ABSTRACT

Background: Literature suggests bipolars may differ in several features according to predominant polarity, but the role of temperaments remains controversial.

Methods: The EPIDEP study was designed to identify bipolar patients among a large sample of major depressives. Only bipolars were included in the current study. Patients were subtyped as predominantly depressive (PD) and predominantly manic and hypomanic (PM) according to a broad (more episodes of a given polarity) and a narrow (2/3 of episodes of one polarity over the other) definition, and compared on their characteristics.

Results: Among 278 bipolars, 182 (79.8%) could be subtyped as PD and 46 (20.2%) as PM (broad definition); the respective proportions were of 111 (81.6%) and 25 (18.4%) using narrow definition. Expanding the definition added little in detecting differences between groups. Compared to PDs, PMs showed more psychosis, rapid cycling, stressors at onset, family history of affective illness, and manic first episode polarity; they also received more antipsychotics and lithium. The PDs showed more chronic depression, comorbid anxiety, and received more antidepressants, anticonvulsants and benzodiazepines. The following independent variables were associated with manic/hypomanic predominant polarity: cyclothymic temperament, first hospitalization ≤ 25 years, hyperthymic temperament, and alcohol use (only for broad definition).

Limitation: Cross-sectional design, recall bias.

Conclusions: Study findings are in accord with literature except for suicidality and mixicity which were related to predominant mania, and explained by higher levels of cyclothymic and hyperthymic temperaments. Temperaments may play a key role in the subtyping of bipolar patients according to predominant polarity, which warrants confirmation in prospective studies.

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1. Introduction

The concept of predominant polarity in bipolar disorders, which can be traced back to the 'late' 70s (Angst, 1978), was forged to define subgroups of patients who mainly experience recurrences of depressive or of manic episodes. It was operationalized by Colom et al. (2006) who proposed a narrow definition requiring a threshold of at least twice as many episodes of one pole of the disorder over the other.

Nevertheless, a broader definition (more episodes of either pole of the disorder) has been suggested (González-Pinto et al., 2010) that seems, according to one study (Baldessarini et al., 2012), as valid as the previous one. Different factors have been associated with predominant mania and predominant depression (Carvalho

et al., 2014), but only two studies reported on affective temperaments as a function of predominant polarity (Henry et al., 1999; Mazzarini et al., 2009). However, these studies yielded controversial findings. The first one (Henry et al., 1999) found that the percentage of manic episodes was positively correlated to hyperthymic temperament scores, whereas the total number of depressive episodes was linked to depressive temperament scores, but negatively correlated to hyperthymic temperament measures. The second study (Mazzarini et al., 2009) did not find evidence for differences in affective temperaments as a function of predominant polarity. However, it is likely that this study had not the power to detect such differences due to the small number of patients included in some of the predominant polarity subgroups.

The current study was therefore designed to (1) assess the prevalence of predominant polarity in a large sample of bipolar spectrum disorder patients, (2) describe the characteristics associated with predominant mania/hypomania and predominant depression in this population, (3) evaluate whether using a

^{*} Corresponding author. Tel.: +33 4 91 70 40 82; fax: +33 4 91 74 55 78.

E-mail address: jazorin@ap-hm.fr (J.M. Azorin).

broader definition may add in detecting differences between predominant-polarity subgroups, and (4) examine into further details the role of affective temperaments with respect to predominant polarity.

2. Methods

2.1. EPIDEP design and general findings

EPIDEP involved 48 specially trained psychiatrists working in 15 different centers in France. It was scheduled in two phases.

In phase 1, 537 patients with major depressive episode (MDE) were recruited by using the Structured Clinical Interview for DSM-IV Axis I Disorder (SCID-P) (First et al., 1996). This instrument is a semi-structured interview which is suitable for clinical studies as it permits clinical judgment to bear on the DSM-IV schema for major depression and other Axis I disorders. Intensity of depression was assessed by the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960); mood disturbances were self-reported by assessing the Multiple Visual Analog Scales of Bipolarity (MVAS-BP) (Ahearn and Carroll, 1996; Hantouche et al., 2001a; Azorin et al., 2012).

In phase 2, scheduled an average of 4 weeks after the first visit, a systematic search for lifetime DSM-IV hypomanic episodes was made through the SCID-P (First et al., 1996) and the checklist of hypomania (Angst, 1992). Sociodemographic characteristics, illness course, family history, comorbidity and information on affective temperaments were also recorded during the second visit. Stressful life events during the 3 months before the original onset of illness were reconstructed as far as possible on the basis of interviews with patients, and their families and hospital records, following the guidelines for assessment of the DSM-IV Axis-IV (American Psychiatric Association, 1994). The age-at-onset was defined as the age at which the patient first met the DSM-IV criteria for the corresponding Axis I disorder; it was obtained from structured interviews with the patients and their relatives and from their medical records. Lifetime comorbidity for Axis I disorders was recorded by using the SCID-P (First et al., 1996). Family history for mental disorders was assessed according to the Research Diagnostic Criteria family history version (FH-RDC) (Andreassen et al., 1977). The FH-RDC is a structured interview method, which is particularly well-suited for collecting family history information, because it provides clinicians with reliable and valid data without adding significant time burden to the assessment process. Finally, self-reporting of affective temperaments (hyperthymic, depressive, cyclothymic and irritable) with four questionnaires was filled out by the patient (Hantouche et al., 2001b). These yes-or-no type questionnaires represent the French version of TEMPS-A (Temperament Evaluation of Memphis, Pisa, Paris and San Diego, autoquestionnaire version); they are designed to quantify temperament in psychiatric patients and healthy subjects (Akiskal et al., 2005).

The study was reviewed and approved by the appropriate ethics committee and patients participated with informed, voluntary, written consent.

EPIDEP was conducted between March 1995 and March 1997.

From the 537 patients included at visit 1, 493 returned at visit 2. Among the latter, 215 were classified as major depressive disorders (MDD), 41 as bipolar (BP) I, 144 as BP II, and 93 as BP not otherwise specified (NOS).

For further details on the methodology and previous findings of EPIDEP, the reader is referred to Hantouche et al. (1998, 2003), Akiskal et al. (2003a, 2003b), Azorin et al. (2012, 2014).

2.2. Patient selection for the present study

Only patients with a diagnosis of BP disorder were included in the current study. We used two different definitions for predominant polarity: a broad definition and a narrow definition. According to the former, patients were considered as predominantly manic or hypomanic (PM) if they had a history of more manic or hypomanic than depressive episodes, and as predominantly depressive (PD) if they had a history of more depressive than manic or hypomanic episodes (González-Pinto et al., 2010). Episodes had to fulfill the DSM-IV criteria for a major depressive episode or a manic/hypomanic episode (American Psychiatric Association, 1994). Using the narrow criteria, manic or hypomanic predominant polarity was defined as at least two thirds of past episodes fulfilling DSM-IV criteria for manic or hypomanic episodes; depressive predominant polarity was defined as at least two thirds of a patient's past episodes fulfilling DSM-IV criteria for major depressive episode (Colom et al., 2006). The patients that did not meet criteria for either definition were excluded from the analysis.

2.3. Statistical analyses

To compare the likelihood of having been exposed to a risk factor among PM patients to the likelihood of exposure among PD patients, raw odds ratios were computed in univariate analyses. A stepwise logistic regression model was then used to identify the factors associated with predominant manic/hypomanic polarity. Based on the results of univariate analyses and variables selected from a literature search, the following were entered into the model: gender, marital status, MVAS-BP total score, psychotic features, alcohol use disorder, other substance use disorder, anxiety disorder, hyperthymic temperament, depressive temperament, cyclothymic temperament, age-at-onset, first hospitalization ≤ 25 years, first episode polarity, rapid cycling, suicide attempts, stressors before illness onset, antidepressants in lifetime, antipsychotics in lifetime, lithium in lifetime, anticonvulsants in lifetime, benzodiazepines in lifetime, electroconvulsive therapy in lifetime, and family history of affective illness. Odds ratios with 95% confidence intervals were used for the observed associations.

3. Results

3.1. Patients

A total of 228 patients who met the broad criteria for predominant polarity were included in the study. Of those, 40 had a diagnosis of BP I disorder, 137 were BP II patients, whereas 51 exhibited antidepressant-associated hypomania (bipolar III) (Akiskal et al., 2003b), the latter being classified as BP NOS according to DSM-IV criteria. Fifty out of 278 BP patients who completed the EPIDEP protocol were excluded from the current study because they did not present any specific predominant polarity according to our definition. The same proportion of PM subjects was observed among BP I and BP II patients (27.5% vs 25.5%, respectively), while BP III patients were by definition predominantly depressive. The mean age of the current study population was 45.54 ± 12.94 years. The mean number of prior episodes was 10.40 ± 12.22 . Multiple hospitalizations were recorded in 40.5%.

Among these 228 patients, 136 met the narrow criteria for predominant polarity. Of those, 19 had a diagnosis of BP I disorder, 80 were BP II patients, whereas 37 were BP III. The same proportion of PM subjects was observed among BP I and BP II patients (26.3% vs 25.0%, respectively). The mean age of this

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