

Lifetime presence of psychotic symptoms in bipolar disorder is associated with less favorable socio-demographic and certain clinical features

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Abstract

Background: The presence of psychotic symptoms in bipolar disorder (BD) is considered a feature of higher severity of illness and, in particular, of manic episodes in bipolar I disorder (BD I). However, the possibility to apply the “with psychotic features” specifier to major depressive episodes in either bipolar II disorder (BD II) or BD I highlights the need for additional research in this area.

Methods: The present study assessed the lifetime presence of psychotic symptoms and related socio-demographic and clinical features in a large sample of BD patients ($N = 360$), with (BDPs, $N = 207$) and without a lifetime history of psychosis (BDNPs, $N = 153$).

Results: An overall less favorable socio-demographic profile was observed in BDPs vs BDNPs. In terms of clinical variables, BDPs vs BDNPs had: earlier age at onset (27.7 ± 10.5 vs 30.1 ± 12.3 years; $p = 0.02$), higher rates of BD I diagnosis (95.7% vs 45.8%; $p < 0.001$), more elevated (manic/hypomanic/mixed) polarity of first (55.2% vs 24.4%; $p < 0.001$) and most recent episode (69.8% vs 35.6%; $p < 0.001$), more comorbid alcohol/substance use disorder (38.1% vs 21.9%; $p = 0.002$), more lifetime hospitalizations (3.8 ± 6.1 vs 2 ± 3 ; $p = 0.002$) and involuntary commitments (1 ± 1.9 vs 0.1 ± 0.4 ; $p < 0.001$), more history of psychosocial rehabilitation (17.9% vs 5.7%; $p = 0.001$), more current antipsychotic use (90.1% vs 70.9%; $p < 0.001$), and lower GAF (62.3 ± 14.2 vs 69.3 ± 12.5 ; $p < 0.001$), but shorter duration of most recent episode (34.1 ± 45.4 vs 50.3 ± 65.7 days; $p = 0.04$), lower rates of comorbid anxiety disorders (23.9% vs 38.2%; $p = 0.005$), and antidepressant use (19.4% vs 56.6%; $p < 0.001$).

Conclusions: The present findings indicate an overall worse profile of socio-demographic and certain clinical characteristics associated with the lifetime presence of psychotic symptoms in bipolar patients.

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1. Introduction

Bipolar disorder (BD) is a chronic and disabling condition, frequently associated with high rates of medical and psychiatric comorbidity as well as high rates of morbidity and mortality for medical causes and suicide [1]. BD is currently classified in two major forms, bipolar I (BD I) and II disorder (BD II), the former associated with manic and, in most cases, depressive episodes, whereas the latter with major depressive and hypomanic episodes. BD II has been traditionally considered a milder form of BD:

however, if this is true with respect to the presentation of elevated mood episodes, the overall burden of illness, particularly in terms of number and severity of depressive episodes as well as suicide attempts, may be as severe (or even more) as in BD II [2].

During both depressive and manic phases of BD, psychotic symptoms may occur [3]. Of note, BD II patients may experience psychotic symptoms and the “with psychotic – mood congruent/incongruent – features” specifier can be applied to major depressive episodes [4].

Nearly half of bipolar patients have a lifetime history of psychotic symptoms [3]. Among these, Schneider's first rank symptoms (e.g., hearing thoughts spoken aloud; hearing voices referring to himself/herself, made in the third person; auditory hallucinations in the form of a commentary, etc.) may occur. These are not necessarily specific to Schizophrenia, as traditionally supposed. Indeed, leading clinicians

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consider psychosis to represent a continuum from schizophrenia to BD [5].

From a clinical point of view, the presence of psychotic symptoms in BD has been associated with a higher severity of illness and a higher morbidity in the long-term [6]. For instance, lifetime psychosis has been associated with poorer prognosis, higher hospitalization rate, more frequent relapses as well as greater functional inter-episodic impairment [6–8]. In particular, Kessing distinguished three groups of bipolar patients: hypomanic, manic with and without psychotic symptoms, finding longer hospitalizations for those with psychosis, with no differences in terms of subsequent relapses [7]. Tohen and colleagues [8] assessed the predictors of recovery and relapse in 166 bipolar patients followed-up for 4 years, observing that predictors of manic recurrences included initial mood-congruent psychosis, lower premorbid occupational status, and initial manic presentation. Furthermore, Coryell and coworkers [6,9], by extending their first study on major depression to 139 manic patients – 90 of whom had psychotic features – found that symptom severity ratings were higher for the latter group. The presence of psychotic features has also been associated with a greater number of weeks ill during follow-up, being the strength of such association similar to that observed among patients with major depressive episodes, reported in an earlier publication [9]. Moreover, psychotic features in manic compared with depressive phases have been associated with greater symptoms severity and higher morbidity in the long-term [6].

In light of the above-mentioned findings, the present study was aimed to assess the lifetime presence of psychotic features and related socio-demographic and clinical correlates in a large sample of Italian bipolar patients.

2. Methods

The sample consisted of 360 bipolar patients, recruited at the University Department of Mental Health of the Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico of Milan, Italy. In order to better represent the phenomenology of BD in the Northern Italian population (Lombardy region), we included patients referred by community-based psychiatric services, including day hospital, outpatient, and inpatient units. All subjects provided written informed consent prior to participation, for having their clinical records reviewed for research purposes. Patients were assessed using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID) [10], which was administered by specifically trained expert psychiatrists. As detected by the SCID, the following conditions were excluded: organic mental disorder, mental retardation, and mental illness secondary to medical disorders.

In order to assess potential residual symptoms, patient's current affective status was assessed using the 21-item

Hamilton Depression Rating Scale [11] and the Young Mania Rating Scale [12]. In addition, the Global Assessment of Functioning (GAF) [13] was administered after the resolution of the most recent mood episode in order to evaluate the individual level of global functioning. Both subjects with or without current pharmacological treatment were recruited.

Socio-demographic and clinical data were collected both on the basis of clinical charts and interviews with patients and their relatives, including: age, age at onset, gender, education, co-habitation, marital status, employment, lifetime occupational functioning impairment (defined as the inability to hold a stable job or to perform tasks at work/work and earn according to the level of education), duration of illness, duration of untreated illness (DUI, defined as the time between the onset of any symptoms of BD and the start of an appropriate stabilizing therapy [14]), duration of most recent episode, lifetime number of psychiatric hospitalizations, lifetime involuntary hospital commitments and suicide attempts, family history of psychiatric disorders, polarity of first and most recent episode, presence of current subthreshold symptoms, history of stressful life-events, lifetime psychiatric and medical comorbidity rates, and lifetime history of psychosocial rehabilitation. Current pharmacological treatment status was also collected, focusing in particular on the use of antidepressants, mood stabilizers, and antipsychotics in mono- and poly-therapy.

All patients were grouped according to the lifetime presence or absence of psychotic symptoms, including hallucinations, delusions, or both.

Multivariate analyses of variance (MANOVA) were used to compare continuous demographic and clinical data across the bipolar subgroups. Chi-square tests were used for categorical socio-demographic and clinical variables. Furthermore, binary logistic regression was performed, including all variables found to be significantly different between the two subgroups as the independent variables and the lifetime presence of psychotic symptoms as the dependent one. A two-tailed significance threshold of $p < 0.05$ was applied, with Bonferroni corrections to account for multiple comparisons. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 22.

3. Results

Socio-demographic and clinical data for the entire sample and related subgroups are provided in Tables 1 and 2.

The MANOVA model proved to be valid (Wilks' lambda test: $F = 4.63$, $p < 0.001$).

In relation to the whole sample, the mean age was 48.6 ± 14.4 years and the male to female ratio was approximately 1:1 (male 47.5%, female 52.6%). The mean age at onset was 28.7 ± 11.4 years and the mean DUI was 58 ± 101.2 months. A positive family history for psychiatric

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