Journal of Affective Disorders 135 (2011) 241–250

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

Phenomenology of psychotic mood disorders: Lifetime and major depressive episode features

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ARTICLE INFO

Article history:
Received 23 June 2011
Received in revised form 29 July 2011
Accepted 29 July 2011
Available online 1 September 2011

Keywords:
Psychosis
Bipolar
Unipolar
Major depression
Mood disorders

ABSTRACT

Background: The nosological and clinical implications of psychotic features in the course of mood disorders have been widely debated. Currently, no specification exists for defining a subgroup of lifetime Psychotic Mood Disorder (PMD) patients.
Methods: A total of 2178 patients were examined, including subjects with Bipolar Disorder (BP) type I (n = 519) and II (n = 207) and Major Depressive Disorder (n = 1452). Patients were divided between PMD (n = 645) and non-psychotic Mood Disorders (MD) (n = 1533) by the lifetime presence of at least one mood episode with psychotic features. Subjects having a depressive episode at the time of assessment were also examined: HAM-D and YMRS scores were compared between MD and PMD subjects, both with and without current psychotic features.
Results: A diagnosis of BP-I, a higher familial load for BP, a higher number of mood episodes lifetime, and a higher prevalence of OCD and somatic comorbidities were all associated to PMD. A diagnosis of BP (OR = 4.48) was the only significant predictor for psychosis. PMD with non-psychotic depression were apparently less severe than MD patients and had a lower rate of "non-responders" to AD treatment. Sub-threshold manic symptoms and suicidal risk were also more pronounced among PMD.
Limitations: The lack of information about number and polarity of previous psychotic mood episodes may be the major limitations of our study.
Conclusions: BP diagnosis is the most significant predictor for psychosis in mood disorders. Non-psychotic mood episodes in PMD patients may be characterized by a distinctive symptom profile and, possibly, a different response to treatment.

1. Introduction

In the late 19th century, Emil Kraepelin described manic–depressive insanity (now called bipolar disorder) and dementia praecox (the modern schizophrenia) as distinct diagnostic entities (Kraepelin, 1921). His dichotomy between

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doi:10.1016/j.jad.2011.07.027

mood disorders and schizophrenia was mainly based on their different illness course and prognosis.

Still now, course and outcome are crucial variables in determining the validity of a diagnostic concept (Robins and Guze, 1970; Feinstein, 1977). However, a lack of convincing support for either categorical or dimensional diagnostic models has progressively moved attention to new domains of psychopathology, where particular patho-physiological disturbances or genetic factors might play a major role (Buchanan and Carpenter, 1994; Flaum et al., 1995; Serretti et al., 2000; Henry and Etain, 2010).

In this sense, the nosological and clinical implications of psychotic features in the course of mood disorders have been widely debated. Currently, psychotic symptoms are considered as a criterion for severity of mood episodes in both Bipolar Disorder (BP) and Major Depressive Disorder (MDD) (A.P.A., 2000). No specification exists for defining a subgroup of lifetime Psychotic Mood Disorder (PMD) patients, though some studies suggest that these patients might share with schizophrenia not only symptom presentation, but also epidemiology (Murray et al., 2004), and, probably, genetic susceptibility (Craddock et al., 2006; Goes et al., 2008; Ivleva et al., 2010). Secondly, where some authors have argued that psychotic features have no validity in terms of prognosis, treatment or family history for mood disorders (Pope and Lipinski, 1978; Maj et al., 1990; Jager et al., 2005), others have found a poorer response to medications (Coryell et al., 1984), a worse short and long-term outcome (Coryell et al., 1982; Coryell et al., 1996; Coryell et al., 2001) and a more severe cognitive impairment (Grant et al., 2001; Hill et al., 2004; Jeste et al., 1996; Glahn et al., 2006). Moreover, while the clinical and prognostic implications of psychotic mania have been extensively explored (Pope and Lipinski, 1978; Coryell et al., 2001; Haro et al., 2006; Canuso et al., 2008), the meaning of psychotic features for depression might have been biased by the separation between unipolar (Coryell et al., 1996; Leyton et al., 1995; Harrow et al., 2000) and bipolar (Guze et al., 1975; Brockington et al., 1982; Mitchell et al., 2001; Parker et al., 2000; Endicott et al., 1985; Tafalla et al., 2009) patients. Indeed, although there is a growing interest in the study of the depressive syndrome by a spectrum-based dimensional approach – *e.g.* see the concept of "*mixed depression*" (Akiskal and Benazzi, 2003; Benazzi, 2000; Benazzi, 2003; Koukopoulos and Koukopoulos, 1999) – most studies on delusional or psychotic depression seem to be implicitly inspired by a polarity-based categorical model, where unipolar and bipolar psychotic depression are referred to as separate constructs. Finally, since most studies on the clinical and severity pattern of depression usually make a comparison between psychotic and non-psychotic patients (Parker et al., 1991; Gaudiano et al., 2008), symptom profile and psychopathological presentation of non-psychotic mood episodes in PMD subjects have not been explored yet.

To address these issues we examined a large multi-center sample in order to detect any demographic and/or clinical feature that might be associated with PMD. PMDs were defined by the presence of at least one mood episode with psychotic features during lifetime, independently from mood polarity. Secondly, we analyzed the phenomenology of a Major Depressive Episode (MDE) with and without psychotic features in both PMD and mood disorder patients with no history of psychotic symptoms (MD). The purpose was to determine whether a lifetime history of psychosis may affect symptom presentation of non-psychotic mood episodes.

2. Methods

2.1. Study sample

Patients were recruited within the context of two large study projects: 1) the Group for the Study of Resistant Depression (GSRD) (started in January 2000) and 2) the COPE Bipolar program (started in December 2003).

The GSRD is a large multicenter, multinational study with the objective of defining some key issues in Treatment Resistant Depression (TRD), such as diagnosis, clinical features and treatment adequacy (for a description of inclusion and exclusion criteria see (Souery et al., 2007, Souery et al., 2011a)). Seven centers have been involved in this project: 1) Department of Psychiatry and Psychotherapy, Medical University of Vienna, Vienna, Austria; 2) Department of Psychiatry, Chaim Sheba Medical Center, Tel-Hashomer, Israel; 3) Department of Psychiatry, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium; 4) Department of Psychiatry, University Hospital Gasthuisberg, Leuven, Belgium; 5) Hôpital la Salpetriere, INSERM U302, Paris, France; 6) Sint-Truiden Psychiatric center, Sint-Truiden, Belgium; 7) Ness-Ziona Mental Health Center, Israel.

The definitions of treatment resistance vary from non response to a single antidepressant given at an adequate dose for sufficient duration (Souery et al., 1999; Thase, 2001; Fava, 2003) to the more complicated failure to respond to two separate courses of treatment with antidepressants from two different classes for adequate duration and dose (Thase, 2001; Committee for Medicinal Products for Human Use CHMP, 2002). For the present study "*non-responders*" were defined as having a HAM-D score higher than 17 after at least 4 weeks of one antidepressant treatment given at an adequate dose.

Regarding the COPE Bipolar program, patients have been recruited within the "Psy Pluriel" center, Centre Européen de Psychologie Médicale (outpatients only), and the department of Psychiatry of Erasme Hospital (in- and outpatients), in Brussels (for a description of the sample see (Souery et al., 2011b)). Briefly, in this program the assessment of mood disorder patients is completed using "COPE-Bipolar.COM" (Clinical Outcome Measures for Bipolar Disorder), a software program consisting on a structured examination tool and immediate data capture. It is composed of ten "modules", each of them dedicated to essential elements of mood disorders, such as socio-demographic characteristics, familiarity, diagnosis, treatment, and quality of life and functioning.

Lifetime and current diagnosis, course of illness and comorbidities were assessed by specifically trained psychiatrists on the basis of the M.I.N.I. interview (Sheehan et al., 1998). Patients were included if they met DSM-IV criteria for a diagnosis of mood disorders (BP-I, BP-II and MDD). Individuals with mental retardation, dementia, neurological disorders or severe organic diseases were excluded. Written informed consent was obtained from all participants in the studies.

Psychiatric familial antecedents were screened by clinical investigation. Positive or negative family history was used as a dichotomous indicator for familial loading using all possible