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Phenomenological subtypes of severe bipolar mixed states: a factor analytic study

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Abstract

Objective: The correct identification of bipolar mixed states (MS) has important implications for clinical practice. The aim of the study was to define the multidimensional psychopathological structure of severe MS. To our knowledge, no factor analytical studies including only patients with MS, have been conducted before.
Methods: In the first week of hospitalization, we evaluated by HAM-D-17, YMRS, BPRS and CGI, 202 Bipolar I inpatients with MS according to *DSM-IV* criteria referred for an ECT trial. A Principal-component analysis followed by Varimax rotation was performed on the 24-item BPRS. The relationships among different symptomatological subtypes and other clinical characteristics were explored.
Results: Six interpretable factors were extracted: *Psychotic-positive symptoms*, *Mania*, *Disorientation-Unusual Motor Behaviour*, *Depression*, *Negative Symptoms* and *Anxiety*. On the basis of the highest z-scores, we found 6 “dominant” BPRS factor groups, that were statistically distinct and without significant overlap in the main symptomatological presentation. Only 29 (14.4%) of our patients could be described as “*Dominant Manic*” and 48 (23.8%) as “*Dominant Depressive*”; most importantly 125 (61.9%) were neither predominately-manic nor predominately-depressive. Variables including age, number of previous episodes, suicidal behavior and HAM-D and YMRS scores significantly differentiated the subtypes.
Conclusion: At least in the most severe forms, MS appears to represent more than the superposition of affective symptoms of opposite polarity. Anxiety, perplexity, psychotic experiences, motor disturbances and grossly disorganized behavior seem to arise from protracted intra-episodic instability and presence of a drive state influencing the mood state and the emotional resonance.
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1. Introduction

Mixed state (MS) refers to an affective condition in which depressive and manic symptoms are simultaneously present. It may manifest as a transitional condition bridging one phase of the illness with another, or it may exist as an independent episode. In the latter case, along with mania and depression, MS represents a major phase of Bipolar Disorder; however, it is often misdiagnosed because of its pleomorphic symptomatological presentation [1] as well as under-diagnosed because of inadequate diagnostic delimitation [2,3].

Definitions of mixed states, especially those with prominent depression, are not well established. There is no terminological uniformity in the literature, and there is a tendency to use such terms as “mixed state,” “mixed mania”, “depression during mania,” and “dysphoric mania” interchangeably. *DSM-IV* and *DSM IV-TR* adopted a pragmatic but restrictive, descriptive approach, requiring full syndromal mania and depression for the diagnosis of MS.

In the last 30 years, a rebirth of interest in MS produced studies of mixed mania [4] (mania plus less than syndromal depression) and, more recently, mixed depression [5] (major depression plus less than syndromal mania). This approach addressed depressive and manic episodes separately, regarding mixed state as subtypes of manic or depressive episodes,

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rather than in terms of specific features or episode components. Manic episodes with or without sub-syndromal depression differ in treatment response, severity of anxiety and course characteristics [6–9]. Although they were not addressed in *DSM-IV*, mixed hypomanic episodes [10] and depressive episodes with concurrent hypomanic symptoms may be common [11–13]. In some patients hypomanic or manic symptoms can be present only during depressive episodes [11,13–15].

As concerns symptomatological features, MS have generally been studied as subtypes of manic or depressive episodes. Symptoms characterizing mixed manic episodes include increased mood lability and irritability, less grandiosity, euphoria, pressure of speech, and decreased need for sleep compared to non-mixed episodes [16]. Dysphoric mood, anxiety, excessive guilt, and suicidality are depressive symptoms associated with mixed-manic episodes [17]. In terms of severity of depression and anxiety, mixed manic episodes were similar to agitated depressive episodes, with more severe agitation, irritability, and cognitive impairment [18].

Irritable mood, distractibility, racing thoughts/flight of ideas, agitation and increased talking are hypomanic symptoms described in mixed depressive episodes [11,19]. Severity of depressive symptoms appears similar in depressive episodes with or without concurrent manic symptoms [13,20]. Anxiety, negative evaluation of self, increased energy, visible hyperactivity, and racing thoughts has been associated with MS, regardless of dominant polarity [21].

Non-affective symptoms, including anxiety or psychosis, could be very common in MS and their role in depressive and manic syndromes may differ. Anxiety scores are correlated with depression scores in mania [21,22] and were minimal in non-mixed mania [18,21]. More recently anxiety has been considered a core symptom of mixed manic episodes [23]. On the contrary anxiety seems to be present in depression, regardless of the presence of mixed features [18]. In bipolar depression, severity of anxiety correlates with manic [21] as well as depressive symptoms [20,21].

In a recent study, conducted on 187 bipolar I inpatients hospitalized for *DSM-IV-TR* acute depressive, manic or mixed episodes, principal factor analysis was performed on 24-item Brief Psychiatric Rating Scale (BPRS 4.0) [24]. The analysis revealed five factors corresponding to "psychosis", "euphoric mania", "mixity", "dysphoria" and "inhibited depression". The mixity factor showed relative independence from "mood symptoms", since it was mainly characterized by a set of symptoms like anxiety, tension, suicidality, and motor hyperactivity that suggest an "anxious-agitated arousal".

Severity of psychosis is not generally increased in mixed versus non-mixed mania [25]. Factorial analyses have delineated a psychotic manic subtype that is distinct from depressive mania [17,26,27]. As with mania, factor analysis of symptoms in bipolar depressive episodes yields a psychosis/delusions factor [28]. Prevalence of psychotic symptoms is lower in depression than in mania, so psychotic symptoms correlate with manic symptoms severity in bipolar depressive episodes [20], as well as with the degree to which affective symptoms are mixed [21]. Psychotic features were more likely to be mood-incongruent in mixed than in non-mixed bipolar depression [1].

Finally in MS, sustained affective instability has been characterized by the "persistent presence of a drive state contradictory to the mood state and/or the emotional resonance" [29] and associated with specific symptoms such as cognitive and motor indecisiveness, emotional perplexity, perceptual disturbances, and a sense of external interference and depersonalization [30]. These characteristics have been considered common in MS [31], and cannot be derived from the superposition of depressive and manic symptomatology and are difficult to be operationalized in a combinatory model.

In the present study we have conducted a factor analysis of BPRS symptoms systematically assessed in a large sample of Bipolar I patients with treatment-resistant MS referred for ECT trial. To our knowledge, this is the first analysis to include only patients with MS diagnosed according to *DSM-IV* criteria. We also explored the relationships between the symptomatological subtypes of MS, identified by means of principal component factor analysis, and other clinical features of mood disorders. Our hypotheses were that 1) in severe mixed states, drive-related "non-affective" symptoms are prominent regardless of manic or depressive symptoms; and 2) the symptomatological presentation might be related to demographic and clinical features.

2. Methods

The study involved 202 Bipolar I patients with treatment-resistant MS, who had received ECT between January 2006 and July 2011 at the Department of Psychiatry of the University of Pisa. The sample comprised 81 males (40.1%) and 121 females (59.9%), with age between 21 and 81 years (mean 44.1, sd = 0.5); 70 (34.7%) were married, 104 (51.5%) single and 28 (13.9%) widowed or divorced. Most of the patients were employed (106, 52.5%), 27 (13.4%) were students, 28 (13.9%) were housewives, and 67 (33.2%) were unemployed or retired.

All subjects met the criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*), for a mixed episode. The diagnoses were made by 2 senior psychiatrists (P.M, M.M.) and were confirmed by the administration of the M.I.N.I. (Mini International Neuropsychiatric Interview-Italian version 5.0.1). When questions arose, all diagnostic information was reviewed for consensus agreement and, if necessary, patients were re-contacted for further clarification. All subjects gave their written informed consent to receive ECT and to participate to this study, and the study was approved by the Ethics Review

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