

Research report

Towards a reconceptualization of mixed states, based on an emotional-reactivity dimensional model

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Abstract

Background: DSM-IV criteria for mixed states may be too restrictive and may actually exclude patients who do not meet the full criteria for a manic and depressive state. Using this DSM-IV definition, many patients who are considered depressed may have mixed features, which can explain why some bipolar depressive states can worsen with antidepressants and can be improved by mood stabilizers or atypical antipsychotics. A dimensional approach not exclusively focused on the tonality of affect would help to define a broader entity of mixed states. The aim of this study was to apply a dimensional model to bipolar episodes and to assess the overlap between the groups defined using this model and using categorical diagnosis.

Method: We assessed 139 DSM-IV acutely ill bipolar I patients with MAThYS (Multidimensional Assessment of Thymic States by Henry et al. in press), a scale that assesses five quantitative dimensions exploring excitatory and inhibition processes, and that is not focused on tonality of mood but on emotional reactivity. We studied the relationship between clusters defined by statistical analyses and DSM-IV bipolar mood states.

Results: This study showed the existence of three clusters. Cluster 1 was characterized by an inhibition in all dimensions and corresponded to the depressive cluster (more than 90% of patients met the criteria for DSM-IV Major Depressive Episode (MDE)). Cluster 2 showed a general excitation and was mainly DSM-IV manic or hypomanic patients (90%). Cluster 3 (Mixed) was more complex and the diagnosis included MDE (56%) in most of the cases associated with manic or hypomanic symptoms, mixed states (18%) defined by DSM-IV criteria, and manic or hypomanic states (25%). Emotional reactivity was relevant to distinguish Cluster 1 (Depressive), exhibiting emotional hypo-reactivity, from Cluster 2 (Manic) and 3 (Mixed), characterized by emotional hyper-reactivity. Sadness was reported equally in all three clusters.

Conclusion: A dimensional approach using the concept of emotional reactivity seems appropriate to define a broad mixed state entity in patients who would be diagnosed with MDE according to DSM-IV. Further studies are needed to test the relevance of this model in therapeutic strategies.

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Keywords: Bipolar disorders; Mixed states; Major depressive episode; Emotional reactivity; Treatment

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1. Introduction

Manic and depressive states are not mutually exclusive and their combination defines the mixed states. Mixed states are common, difficult to treat, potentially severe, and may carry a high risk of suicide (Dilsaver et al., 1994; Vieta, 2005a). However, mixed states are very heterogeneous entities and this broad diversity is illustrated by the reported rates among manic patients, from 14 to 67% (Akiskal et al., 1998). For Kraepelin (1913), the concept of mixed state was broader than that defined in the current classifications (for the evolution of the mixed states concept see Marneros, 2001). Kraepelin described 6 mixed states, from manic states with dysphoric features to depressive states with some agitation. Currently, some authors use the concept of “mixed depressive state” or “agitated depression” to describe “soft” mixed states defined by a depressive state associated with manic or hypomanic symptoms (Koukopoulos and Koukopoulos, 1999; Benazzi, 2002; Akiskal et al., 2005). However, there is no definition in the current classifications that distinguish this “soft” mixed state. Suppes et al. (2005) have recently identified mixed hypomania as a common type of episode within the bipolar spectrum. Akiskal and Benazzi (2005) also showed the existence of dysphoric hypomania and discussed the interest of categorical and dimensional conceptualizations of a broad spectrum of mixed states. Therefore, to meet the criteria for a mixed state using the DSM-IV, a patient should have a full manic state associated with a depressive episode. More precisely, to fulfill the criteria for a manic episode the mood must be exalted and this mood state must be associated with three symptoms, or four if the mood is irritable. If a patient met the criteria for a depressive episode in combination with an irritable mood but if this were associated with only three symptoms of mania, he would not meet the criteria for a mixed state. He would only meet the criteria for a depressive episode. Thus, a single symptom is sufficient to shift from one affective state to another, along with the corresponding change in treatment strategy. A categorical approach does not allow for the classification of all these states on a continuum. As suggested by some authors (McElroy et al., 1992, 1995; Bauer et al., 1994), a dimensional model could be helpful to better characterize mood states in bipolar disorders and more particularly, those with an admixture of manic and depressive features. In 1997, Perugi and colleagues operationalized new mixed state criteria in part based on the concept of emotional instability and they showed that mixed states were more frequent than expected using the DSM-IV.

Based on the Kraepelinian concept of mood states, we built a tool called MATHyS (Multidimensional

Assessment of Thymic States) to define mood states as the function of a dimensional approach (Henry et al., *in press*). Kraepelin defined mood states as starting from excitement or inhibition of the three domains of psychic life: cognitive processes (train of thought rather than its contents), mood, and volition (expressed in psychomotor activity). We extended this by changing the tonality of mood (sadness vs. euphoria) for emotional reactivity (hypo- vs. hyper-reactivity), which is closer to the concept of dimensions. An emotion is characterized by its tonality (pleasant/unpleasant) and also by its intensity (the arousal) (Lang, 1995).

The dimensions assess inhibitory or excitatory processes; therefore they can be applied to manic or depressive states and to states presenting with an admixture of both. Emotional reactivity may be considered as a new component in the comparison of current mood scales. The goal of this dimension is to discriminate mood states as a function of emotional reactivity rather than based exclusively on the tonality of mood (euphoria/depressive mood).

The aims of this study were: 1) to conduct a cluster analysis using a dimensional approach in order to explore the clinical heterogeneity of bipolar states, 2) to assess the relationship between the different clusters and the diagnoses using the DSM-IV criteria, 3) to describe the dimensional profile of each cluster and more particularly to test the relevance of emotional reactivity to define mood states, and particularly mixed states.

Our hypothesis was that mixed states correspond to a broader entity than those defined in DSM-IV and that a definition based on the tonality of mood may fail to capture this heterogeneity, whereas a definition based on emotional reactivity may be more appropriate. The validity of a broader definition of mixed states may have therapeutic implications because episodes currently considered as depressive states may actually qualify to be mixed states, and may respond well to primarily anti-manic treatment, and poorly to antidepressants.

2. Methods

2.1. Patients

Bipolar patients ($n=139$) were recruited from consecutive inpatient admissions in a general psychiatry unit, and from outpatients in a specific consultation for bipolar disorders (Charles Perrens Hospital, Bordeaux).

Patients were interviewed by a trained psychologist using the French version of the Diagnosis Interview for Genetic Studies (Nurnberger et al., 1994) for DSM-IV diagnosis (APA, 1994). We focused on the part assessing

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