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COMMENTARY

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On the centrality of mixed features in mood disorders: Listening to Kraepelin and Weygandt and moving forward

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DSM-5 Mixed Features Specifier (DSM5-MFS) is a nosological improvement over DSM-IV, in that it allows clinicians and researchers to more accurately characterize patients who experience concurrent symptoms of mania/hypomania and depression, but is not an advance over historical conceptualizations of mixed states.

Kraepelin and Weygandt considered any recurrent mood state, be it depressive or manic, as part of one single illness: manic-depressive insanity (MDI).[1,2] It was the recurrence of affective episodes, alternating with euthymia, that allowed a diagnosis of MDI, even for individuals who experienced only depressive episodes. In Kraepelin's approach, mixed states were conceptualized as a frequent and central core of MDI.[3] Later, Leonhard[4] distinguished between subjects with bipolar and unipolar disorders, based on genetic and course findings, leading to the bipolar/unipolar dichotomy, which was then endorsed in DSM-III and DSM-IV and which, we believe, has indirectly created a barrier to appropriate recognition of mixed states. By definition, mixed states imply the co-existence of the two poles, which makes it difficult to found the pillars of mood disorder classification on the separation between depressive and manic-bipolar disorders, as DSM-III and -IV have done. Conversely, Kraepelin thought that mixed states were frequent and did not put polarity at the foundation of mood illness diagnosis.[2]

Indeed, several studies have shown that mixed features are common in both major depressive disorder (MDD) and bipolar disorder and have challenged the classic MDD-bipolar disorder dichotomy, highlighting the need to bridge the gap between the two disorders.[2] DSM-5 has made a tentative, yet significant, step in that direction. In fact, the manual has extended the possibility to apply DSM5-MFS to subjects with MDD, in addition to subjects with bipolar I and bipolar II disorders, this latter being another change from DSM-IV. However, the threshold for DSM5-MFS has been established at a level that, in our opinion, remains excessively high and excludes patients with key mixed syndromes, both in the bipolar and MDD fields.

Not only is it impossible to apply DSM5-MFS to those patients who endorse a major affective episode along with only one or two concomitant symptoms of the opposite pole, but DSM5-MFS is inapplicable also to those whose opposite pole symptoms are represented by psychomotor agitation, distractibility or irritability, who, in our opinion, are those that are closer to the mixed state core. Neglecting these features prevents the description and categorization of very important and frequent clinical pictures, which we believe are key for research and for clinical practice. For instance, Goldberg and colleagues[5] found that two-thirds of the 1380 individuals who met criteria for bipolar I or II depressive episodes at entry into the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) trial endorsed concomitant manic symptoms, most often distractibility, flight of ideas or racing thoughts, and psychomotor agitation. Those subjects were significantly more likely than those with "pure" depressive episodes to have early age at illness onset, rapid cycling, bipolar I subtype, history of suicide attempts, and more days in the preceding year with irritability or mood elevation. Interestingly, only 14.8% of the 1380 study subjects met full criteria for DSM-IV mixed episodes and only 31.2% had a depressive episode with no manic symptoms, whereas 54% endorsed one, two, or three concomitant manic symptoms, with the great majority of the latter endorsing "only" one or two manic symptoms. Using the DSM-5 classification, most of these subjects would not be identified with the MFS, because of not endorsing at least three concomitant manic symptoms or because of endorsing symptoms such as psychomotor activation, distractibility or irritability, which do not count towards the attribution of such a specifier.

Clearly, DSM-5 does not provide the possibility to improve the ability of clinicians and researchers to identify, categorize, study and differentially treat subjects with the clinical pictures described above.

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For instance, DSM-5 does not offer the possibility to distinguish between a patient with a purely depressive episode and a patient with depression, psychomotor agitation, distractibility, irritability and two other manic symptoms.

We completely subscribe to Malhi *et al.*'s recommendation[1] to consider activity as a key dimension of mixed states and we disagree with DSM-5's exclusion, mostly based on a nonspecificity assumption, of psychomotor agitation, distractibility and irritability as valid criteria for an MFS. As it currently stands, a diagnosis of DSM5-MFS relies on criteria such as euphoric mood, grandiosity, decreased need for sleep and impulsive pleasurable behavior, which are rare in mixed depressive episodes, while paradoxically excluding symptoms such as psycho-motor agitation, distractibility and irritability, which are central features of mixed depression.[2]

We also agree with the Mood Assessment and Classification (MAC) Committee about the fact that mixed states are heterogeneous and may benefit from a more dimensional nosography and from a greater degree of attention, at least in terms of research studies, to symptom structure and symptom clusters, as a means to better identify clinically relevant phenotypes and to enable the identification of more homogenous samples for genetic, imaging and treatment studies. Indeed, Weygandt's classification of mixed states[1] might be a good starting point for further research towards an approach that is closer to clinical reality and to research and clinical needs.

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REFERENCES

1. Malhi GS, Berk M, Morris G, et al. Mixed mood: the not so United States?. *Bipolar Disorders*. (in press).
2. Koukopoulos A, Sani G, Ghaemi SN. Mixed features of depression: why DSM-5 is wrong (and so was DSM-IV). *British Journal of Psychiatry*. 2013;203:3-5.
3. Salvatore P, Baldessarini RJ, Centorrino F, et al. Weygandt's on the mixed states of manic-depressive insanity: a translation and commentary on its significance in the evolution of the concept of bipolar disorder. *Harvard Review of Psychiatry*. 2002;10:255-275.
4. Leonhard K. *Aufteilung der endogenen Psychosen und ihre differenzierte Ätiologie [Distribution of Endogenous Psychoses and their Differentiated Aetiology]*. Berlin: Akademic-Verlag; 1957.
5. Goldberg JF, Perlis RH, Bowden CL, et al. Manic symptoms during depressive episodes in 1,380 patients with bipolar disorder: findings from the STEP-BD. *American Journal of Psychiatry*. 2009;166:173-181.

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