The frontier between residual and subsyndromal symptoms in bipolar disorder: revisiting concepts and discussing clinical relevance

Gabriela Léda-Rêgo,1,2 Mirna Scippa,1,2,3

Since bipolar disorder (BD) was first described, clinicians and researchers have been trying to help patients to overcome it and lead fulfilling lives. However, satisfactory clinical control is still rarely achieved: most individuals with BD require maintenance treatment to prevent new episodes and restore quality of life.1 Although it has been observed that BD patients undergo different phases according to treatment response, the literature describes them with inconsistent terminology, and we would like to reflect on the effects of this confusion.

From this perspective, there has been growing awareness of the need to determine a state of remission or euthymia. Therefore, we begin with a presentation of the basic concepts and recovery phases in the figure below.2

An interesting recent study by Rocha & Correia3 pointed out that, despite some recommendations, there is no precise description of the state of euthymia, which has led to widely varying definitions across studies. In fact, the remission cut-off points found in literature usually range from 6 to 14 for the Hamilton Depression Rating Scale, and from 6 to 12 in the Young Mania Rating Scale. Additionally, satisfactory clinical control is rarely achieved in BD: patients frequently maintain residual psychopathology, even in “euthymia,” which raises questions about the validity of this concept.

Moreover, we would like to draw attention to another relevant problem: we have observed that subsyndromal and residual terms are being confused. Clinicians and researchers only assess remission through total score thresholds, most often either the Hamilton Depression Rating Scale, the Bipolar Depression Rating Scale, the Young Mania Rating Scale or the Montgomery-Asberg Depression Rating Scale without referring to the recommended definition of syndrome. Although there might be several difficulties in measuring syndromal aspects in clinical and research practice, what does a single total score say in terms of clinical relevance?

Considering that the cumulative evidence points to the overwhelming impact of residual and/or subsyndromal symptoms on functional outcome levels4 and that their reduction is an important target for preventing relapse/recurrence, how can we precisely target these symptoms if we do not discriminate their boundaries? What is their real impact? How can we adapt pharmacological and psychosocial therapeutic strategies to the specific case?
No clear approach about how to validate these terms has been presented. We continue to see a gap between euthymia and recovery and a failure to distinguish between residual and subsyndromal symptoms, which indicate that we still have much to learn about scientific methodology. Thus, there is a need to standardize these terminologies, not just to facilitate comprehension of the disorder’s evolution, but to enable comparisons between studies. By refining the dialogue between clinical and research practice, finer-grained management strategies can be developed. Finally, in light of the above, we suggest that greater effort should be made in this direction.

Disclosure

The authors report no conflicts of interest.

References

1. Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord. 2018;20:97-170.

2. Tohen M, Frank E, Bowden CL, Colom F, Nassir Ghaemi S, Yatham LN, et al. The International Society for Bipolar Disorders (ISBD) task force report on the nomenclature of course and outcome in bipolar disorders. Bipolar Disord. 2009;11:453-73.

3. Rocha PM, Correa H. Is it time for psychiatry to discuss consensus criteria for euthymia? Clinical, methodological, research, and ethical perspectives. Braz J Psychiatry. 2019;41:97-8.

4. Gitlin MJ, Miklowitz DJ. The difficult lives of individuals with bipolar disorder: a review of functional outcomes and their implications for treatment. J Affect Disord. 2017;209:147-54.

Figure 1 Illness stages in bipolar disorder (adapted from Tohen et al.2). BDRS = Bipolar Depression Rating Scale; CGI = Clinical Global Impression; HAMD-17 = Hamilton Depression Rating Scale; MADRS = Montgomery-Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale.