Treatment-resistant mood disorders

Ives C. Passos1,2,3, João Quevedo1,2,4

1 Center of Excellence on Mood Disorder, Department of Psychiatry and Behavioral Sciences, The University of Texas Science Center at Houston, Houston, Texas, USA.
2 Center for Translational Psychiatry, Department of Psychiatry and Behavioral Sciences, The University of Texas Science Center at Houston, Houston, Texas, USA.
3 Bipolar Disorder Program and Laboratory of Molecular Psychiatry, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil.
4 Laboratory of Neurosciences, Graduate Program in Health Sciences, Health Sciences Unit, University of Southern Santa Catarina, Criciuma, SC, Brazil.

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Treatment-resistant mood disorders pose a great socioeconomic and life-threatening burden on public health system. On one hand, major depressive disorder (MDD) has a lifetime prevalence of 17-21%, and it is a leading cause of disability adjusted life years worldwide accordingly to ‘The Global Burden of Disease’ study1. However, only 30-40% of patients achieve remission following a standard trial with a first-line antidepressant agent2. On the other hand, bipolar disorder (BD) affects about 2% of the world’s population, with subthreshold forms affecting another 2%3. It is known that non-response in bipolar depression is also highly prevalent, and it occurs in 40% of patients4. Moreover, the addition of antidepressants to an ongoing treatment with mood stabilizers will be helpful in only a quarter of patients with bipolar depression5. It is also known that the rates of completed suicide in patients with BD are 7.8% in men and 4.9% in women6, which could be partially explained by treatment refractoriness. Therefore, despite the pharmacological and psychological strategies to treat patients with mood disorders, how to treat the large number of patients who are refractory to them is still a major challenge. Lack of such knowledge is an important question since treatment-resistant mood disorder patients are associated with greater morbidity, suicide attempts, as well as with extensive use of mood-related and general medical services7. Thus, a book on the subject of treatment resistance is key and of great clinical and public health value.

The book “Treatment-Resistant Mood Disorders”8 covers the forefront findings in this issue and provides a detailed outline of current therapeutic strategies and future therapeutic targets. It stands out as an essential tool for clinicians and researchers. The first chapters of the book looking for enlighten the reader about the current definitions of refractory mood disorders, as well as aspects related to epidemiology and assessment. Notwithstanding the lack of a clear consensus on a working criteria for treatment resistance mood disorders, several key parameters have been agreed, including the multi-dimensional assessment of the symptoms severity, presence of psychiatric or general medical comorbidity, and the objective determination of previous response to adequate treatments. One interesting point presented by the book is the comorbidity with anxiety disorders, such as posttraumatic stress disorder and panic disorder, which are common among treatment-resistant patients8-9. The likelihood of remission in anxious depression was only one third compared with those having pure depression for instance10. Besides refractoriness to antidepressants and mood stabilizers, patients with comorbidity anxiety disorders are also associated with functional impairment, poor psychosocial adjustments, more frequent hospitalizations, increase suicidality, and slower recovery from a mood episode10,11,12.

Both chapters of predictors of treatment response in MDD and BD cover the substantial progress that has been made over the last few years in the search for clinically useful variables. In this vein, a recent work has led to the development of a risk stratification tool for treatment resistance in MDD incorporating both baseline socio-demographic and clinical features11. The study was innovative because of the use of machine learning techniques to analyze several variables at the same time leading to a useful predictive tool to assess treatment resistance. However, clinical information alone probably is insufficient for adequate prediction. Genetics and neurobiological markers may help to improve the accuracy of the clinical predictive tools. For instance, a large study including 1761 bipolar type-1 patients from the Taiwan Bipolar Consortium showed that two single nucleotide polymorphism located in the introns of GAD1 gene (rs17026688 and rs17026651) were strongly associated with the response to lithium maintenance treatment13. Therefore, future studies may combine clinical, genetic, epigenetic, neuroimaging, and/or neurobiological markers to obtain meaningful signatures to predict treatment response and provide a more personalized treatment12. Advanced pattern recognition methods, such as machine learning techniques, that could integrate these characteristics may be of great value in this challenge.

The book also supplies updated data about evidence-based pharmacological and psychosocial approaches for treatment-resistant mood disorder, as well as about the use of electroconvulsive therapy, which remains one of the most important tools available. The chapter about evidence-based pharmacological approaches for treatment-resistant depressive disorder is one of the most important for clinical practice, since it provides a detailed and concise overview of the augmentation and switching pharmacological strategies in MDD. Other strategies of non-invasive, such as transcranial magnetic stimulation (TMS), and invasive neurostimulation, such as deep brain stimulation, are also addressed in subsequent chapters. Moreover, the last two chapters provide meaningful information on potential novel therapeutic targets for mood disorders, such as the pathophysiological findings in the glutamatergic and immune system. In this vein, the fast-acting antidepressant Ketamine arises as an option in severe and refractory patients with MDD. Also, the better understanding of the latter pathophysiological mechanism could shed some light on how to address cognitive and functional impairment associated to the illness progression that take place in some patients10.

In summary, the book “Treatment-Resistant Mood Disorders” provides a much-needed overview of all current aspects related to treatment resistance in the mood disorders. It, therefore, will be of great value to clinicians, researchers, and public health officials in helping to fundamentally advance the field of psychiatric refractory treatment.

References


