Introduction

Unresolved Questions About Treatment-Resistant Anxiety Disorders

By Dan J. Stein, MD, PhD, and Soraya Seedat, MB ChB, FC Psych (SA)

Anxiety disorders are the most prevalent psychiatric disorders in both developed and developing regions around the globe. They are also enormously costly, both in terms of individual suffering and impairment and direct medical and indirect social costs. Part of the reason for these high costs is that anxiety disorders are typically underdiagnosed and undertreated.

Physicians who frequently diagnose and manage anxiety disorders will also be familiar with the prevalence and cost of another phenomenon: treatment-resistant anxiety disorders. Despite enormous strides in recent understanding and management of anxiety disorders, first-line treatments are not effective for all patients. Even in those patients who experience a treatment response, remission of symptoms may not be seen. Treatment-resistant anxiety disorders have, however, received relatively little attention from researchers. Several questions remain unresolved, beginning with how best to define treatment resistance. It remains important to develop consensus on the operationalization of partial response, response, remission, and recovery for each anxiety disorder. Similarly, it is crucial to develop a consensus on different levels of nonresponse, ranging from the failure to respond to first-line pharmacotherapy or psychotherapy, to the failure to respond to a comprehensive series of interventions.

A second question is the underlying psychobiology of treatment resistance. In order to address this issue we need to better understand the heterogeneity of each of these conditions. In obsessive-compulsive disorder (OCD), for example, patients with obsessional slowness and hoarding, tics and neurological soft signs, and comorbid schizotypal personality disorder may be less likely to respond to first-line interventions. Particular OCD subtypes may well have specific biological correlates.

Research on anxiety disorders is fortunate to have excellent animal models on which to draw. It is less clear, however, how to address the more clinical concept of treatment resistance in basic paradigms. There is now some attention to such issues. OCD with comorbid tics, for example, is a clinical phenomenon associated with treatment resistance to selective serotonin reuptake inhibitors. Basic research on the striatum may in time contribute to understanding the relevant underlying mechanisms.

A third question is the key clinical one of how best to intervene in treatment-resistant anxiety disorders. The number of randomized controlled trials for refractory anxiety disorders is extraordinarily limited. Fortunately, there has been some recent attention to this gap. In OCD, there have been several controlled trials of antipsychotics as augmenting agents in patients resistant to treatment with selective serotonin reuptake inhibitors. Interest in a number of other interventions, including combining or switching treatment modalities, is also becoming apparent.

Given the importance of the existing questions about treatment-resistant anxiety disorders and the recent interest in addressing them, an issue on this subject was timely. We wish to express our thanks to the contributors for their thoughtful pieces on generalized anxiety disorder (Moira Rynn, MD, and Olga Brawman-Mintzer, MD), panic disorder (Borwin Bandelow, MD, PhD, and Eckart Rüther, MD), posttraumatic stress disorder (Mark B. Hamner, MD, and colleagues), and social anxiety disorder (Michael Van Ameringen, MD, and colleagues).

REFERENCES


Dr. Stein is professor of psychiatry and Dr. Seedat is associate professor of psychiatry at the Medical Research Council Unit on Anxiety and Stress Disorders in the Department of Psychiatry at the University of Stellenbosch in Cape Town, South Africa.