

Introduction

Management of Treatment-Resistant Depression

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This supplement provides several perspectives on managing treatment-resistant depression. Methods to recognize, define, and assess treatment-resistant depression have been presented previously.¹ Additionally, in these pages you'll find substantive reviews of the available evidence for treatment options available if the first (or subsequent) treatment step(s) does not provide the desired outcome (i.e., full symptomatic remission and functional restoration).

Maurizio Fava, M.D., provides a very thorough review of the options of adding a second antidepressant to the initial medication (combination) or adding a second medication that is not recognized as an effective antidepressant, e.g., buspirone or triiodothyronine (T₃), to the initial antidepressant (augmentation).

While augmenting or combining medications may be suitable for many patients (especially those who both tolerate and benefit to some degree from the initial treatment), switching to a different antidepressant may be preferred in patients who do not tolerate or respond minimally to the initial antidepressant. Lauren B. Marangell, M.D., provides an in-depth look at the available evidence that guides switching strategies.

Michael E. Thase, M.D., and colleagues detail the multiple roles that may be played by psychotherapy in the management of depression, including enhancing effectiveness, reducing symptoms, restoring function, or even reducing relapse/recurrence rates. Important new studies are reviewed that illuminate the cases in which the combination of medication and psychotherapy is especially useful, such as chronic depressions or depressions that have responded, but not fully remitted, to medication monotherapy.

Madhukar H. Trivedi, M.D., and Beverly A. Kleiber, Ph.D., highlight the apparent potential advantages of systematic step-by-step treatment sequences (algorithms or clinical pathways). Investigations to better define empirically the next "best" steps are ongoing, as are studies that compare the clinical outcomes and costs of algorithm-driven treatment with treatment-as-usual. Their report also discusses the potential utility of clinically acquired symptom measures to better guide and optimize the benefits of each treatment step.

We are still far from being able to recommend a specific treatment sequence for one or another type of depression (or types of prior treatment resistance). Conversely, it would appear that the conscientious application of the available treatments holds substantial promise for increasing both response and remission rates in difficult-to-treat depressions.

Finally, due to space limitations, this supplement does not detail highly effective, established approaches for treatment-resistant depression such as electroconvulsive therapy, nor does it specify potential new treatments that are under investigation, such as substance P antagonists,² transcranial magnetic stimulation (TMS),³ or vagus nerve stimulation (VNS).⁴ However, the thorough, evidence-based reviews presented here do provide a comprehensive, clinically useful synopsis of pharmacologic and psychotherapeutic approaches in the management of treatment-resistant depression. While knowledge in the optimal management of these most difficult depressions will expand dramatically over the next several years, this supplement clearly specifies the available evidence to help inform current clinical practice.

REFERENCES

1. Rush AJ, Fava M, Marangell LB, et al. Managing treatment-resistant depression. *J Clin Psychiatry Audiograph Series* 2001;4(4):2-14
2. Kramer MS, Cutler N, Feighner J, et al. Distinct mechanisms for antidepressant activity by blockade of central substance P receptors. *Science* 1998;281:1640-1645
3. George MS, Belmaker RH, eds. *Transcranial Magnetic Stimulation in Neuropsychiatry*. Washington, DC: American Psychiatric Press; 2000
4. George MS, Sackeim HS, Marangell LB, et al. Vagus nerve stimulation: a potential therapy for resistant depression? *Psychiatr Clin North Am* 2000; 23:757-783

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