Treatment of Depression Versus Treatment of PTSD

Steven D. Hollon, Ph.D.

Two articles in this issue, one on the treatment of depression (what to do when the initial modality does not work) and the other on the treatment of posttraumatic stress disorder (PTSD) (the impact of choice with respect to type of treatment), speak to important clinical issues, and together they provide an opportunity to think about similarities and differences across the two disorders. I comment first on the depression article and then the one on PTSD before concluding with a comment on the ways in which the treatment literatures for these disorders differ and what those differences might mean.

Treatment of Depression

In their article in this issue, Dunlop and colleagues (1) focus on what happens when patients who do not remit after being treated with cognitive-behavioral therapy (CBT) or an antidepressant medication receive augmentation with the other monotherapy so as to step them up to combined treatment. The authors note that it would not be appropriate to draw causal inferences from the study given that different patients are likely to complete and respond to the different interventions. Randomization is used to offset selection bias in randomized controlled trials, but the subsets of patients who do not respond to the different treatments are likely to be quite different from one another, so direct comparisons are prone to bias. In keeping with current convention, response refers to a 50% reduction in symptoms, remission refers to a normalization of symptoms, relapse refers to the return of the treated episode, and recovery refers to the end of the underlying episode (2). The authors make some interesting observations: 1) combined treatment was associated with higher rates of response and remission after lack of response or remission to either monotherapy; 2) remission rates were generally higher when an antidepressant medication was used to augment prior CBT (which did somewhat less well than antidepressant medication during the initial round of treatment) than when CBT was added to prior antidepressant medication, although the rates of response did not differ; and 3) higher levels of anxiety both at baseline and prior to augmentation predicted poorer outcomes in either sequence.

The question guiding such studies is what to do next when the initial monotherapy is not enough. There is a growing consensus that remission should be the goal of treatment, not just response (2). Highly trained research psychiatrists typically dose to remission, pushing the dosage as high as needed until remission is achieved or dosage-limiting side effects are encountered and then either augmenting (in the case of partial response) or switching (in the case of nonresponse), often to another medication class, until remission is achieved (3). Much of what passes for antidepressant medication treatment nowadays is done by general practitioners who either undermedicate their patients or keep them on the same medication far too long, when all that is achieved is response and not remission (4). Dunlop et al. are to be commended for pushing their medication dosages high enough to bring about remission (when it was possible) for that patient. Patients who did not remit on CBT were later given only a quarter "dose" of CBT when they were augmented with antidepressant medication (in contrast, patients who did not remit on antidepressant medication were kept on the full dosage of that medication when augmented with CBT); rates of response and remission were somewhat lower for that sequential combination, and that could have been an artifact of the less than full version of combined treatment that was provided. The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study found little difference between augmenting and switching across four successive treatment steps; doing so was associated with a near doubling of the cumulative remission rate (from 37% to 67%) (5), although as in the Dunlop et al. study, that increment could not be attributed to either switch or augmentation in the absence of a control condition. That being said, something must be done for patients who do not remit or even respond, and stepping them up to combined treatment by virtue of adding the other monotherapy is as reasonable a choice as any (6).

Treatment of PTSD

In their study of PTSD treatment in this issue, Zoellner and colleagues (7) focused on whether choice of modality worked to enhance response to treatment, or at least adherence to and completion of treatment. The authors implemented a doubly randomized design in which patients were shown videos describing prolonged exposure and sertraline treatment and then asked to indicate their treatment preference before being randomly assigned either to be treated with their preferred choice or to undergo a second randomization to one or the other treatment. In brief, patients preferred prolonged exposure over antidepressant medication (61% compared with 39%), and those who got their preferred modality were

more likely to adhere to treatment and to no longer meet criteria for PTSD. Considerable gains were evident for both treatments; such differences as were evident favored prolonged exposure over antidepressant medication. The findings indicate both that prolonged exposure is efficacious in the treatment of PTSD and that choice is to be preferred over its absence. Gains were largely maintained across a 24-month follow-up, with responders to prolonged exposure offered up to two booster sessions, whereas nearly all of the antidepressant medication responders were kept on medication.

Similarities and Differences in Treatment of Depression Versus PTSD

The first thing that strikes me with respect to these two literatures is the greater focus on relapse (the return of the treated episode) and recurrence (the onset of wholly new episodes) in the depression literature and the relative lack of attention to this issue in the treatment literature on PTSD. If and when antidepressant medication is efficacious in the treatment of depression, it only works for as long as it is taken, and symptom return is a common and concerning issue. Patients treated to remission with CBT are less than half as likely to relapse after treatment termination as patients treated to remission with antidepressant medication (8). Although I am no expert when it comes to PTSD, from what I have seen, there is little attention to this issue in the PTSD literature, although perhaps there should be. CBT has rarely been compared with antidepressant medication in the treatment of PTSD, but in one relevant study trauma-focused therapy (in this instance, eye movement desensitization and reprocessing) had an enduring effect not found for antidepressant medication (9). Relapse and recurrence are common in depression (prior exposure to CBT cuts their rates by more than half but does not eliminate them altogether), and they would appear to be problematic with respect to PTSD after termination of antidepressant medication but seem rarely addressed in this literature (patients were kept on antidepressant medication for the duration of the follow-up in the Zoellner et al. PTSD study). The question is whether trauma-focused CBT for PTSD actually eliminates the risk for the return of symptoms after treatment termination. The initial indications (both from the study just cited [9] and from the Zoellner et al. study] are that it might. That is incredibly important if true, and it deserves to be pursued in further CBT/antidepressant medication comparisons that follow remitted patients after treatment termination. It is possible that trauma-focused CBT has an enduring effect lasting beyond the end of treatment that is not found with antidepressant medication, which appears to be merely symptom suppressive, as is the case in depression. It also could point toward an underlying difference in the nature of the two disorders that would be important in its own right but for different reasons (depression may be inherently recurrent, whereas PTSD is the consequence of some intervening event that no longer holds sway once that consequence is addressed). Freud was first to note that the essence of depression (and the thing that separates it from grief) is the diminished sense of self (negative self-concept) that often predates the onset of the disorder (10). While treatment may succeed in turning back the symptoms, anyone who has ever been depressed is at three to five times greater risk of becoming depressed again than someone who has never been depressed (11). If someone is prone to self-doubts, those beliefs go with them into every situation and can be triggered by any reversal of fortune in life, usually involving either love or work. PTSD is always triggered by some external event that happens to someone. Patients may take it to heart, but it is not the essence of the self. I have heard it said by trauma-focused therapists that although their patients can be traumatized again, once a given trauma is adequately treated, the symptoms typically do not come back in the absence of new trauma.

The second thing that strikes me is the lack of specificity in our psychological treatments of response to depression, in that spontaneous remission and nonspecific processes account for the bulk of the acute response to treatment among nonpsychotic patients (12), as opposed to PTSD, in which treatment response (other than the symptom-suppressing response to antidepressant medication just described) is largely specific to trauma-focused treatment (13). As above, it is not clear whether this is a consequence of patients (PTSD may simply differ from depression) or procedures (trauma-focused CBT for PTSD may simply cut "closer to the bone" than CBT for depression), but that is another question that deserves to be explored.

AUTHOR AND ARTICLE INFORMATION

The Department of Psychology, Vanderbilt University, Nashville, Tenn.

Send correspondence to Dr. Hollon (steven.d.hollon@vanderbilt.edu).

The author reports no financial relationships with commercial interests.

Accepted February 15, 2019.

Am J Psychiatry 2019; 176:259–261; doi: 10.1176/appi.ajp.2019.19020173

REFERENCES

1. Dunlop BW, LoParo D, Kinkead B, et al: Benefits of sequentially adding cognitive-behavioral therapy or antidepressant medication for adults with nonremitting depression. Am J Psychiatry 2019; 176:275–286
2. Rush AJ, Kraemer HC, Sackeim HA, et al: Report by the ACNP Task Force on response and remission in major depressive disorder. Neuropsychopharmacology 2006; 31:1841–1853
3. Hollon SD, DeRubeis RJ, Fawcett J, et al: Effect of cognitive therapy with antidepressant medications vs antidepressants alone on the rate of recovery in major depressive disorder: a randomized clinical trial. JAMA Psychiatry 2014; 71:1157–1164
4. Hollon SD, Cohen ZD, Singla DR, et al: Recent developments in the treatment of depression. Behav Ther (in press)
5. Rush AJ, Trivedi MH, Wisniewski SR, et al: Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. Am J Psychiatry 2006; 163: 1905–1917
6. Hollon SD, Jarrett RB, Nierenberg AA, et al: Psychotherapy and medication in the treatment of adult and geriatric depression: which

monotherapy or combined treatment? J Clin Psychiatry 2005; 66: 455–468
7. Zoellner LA, Roy-Byrne PP, Mavissakalian M, et al: Doubly randomized preference trial of prolonged exposure versus sertraline for treatment of PTSD. Am J Psychiatry 2019; 176:287–296
8. Cuijpers P, Hollon SD, van Straten A, et al: Does cognitive behavior therapy have an enduring effect that is superior to keeping patients on continuation pharmacotherapy? A meta-analysis. BMJ Open 2013; 3:e002542
9. van der Kolk BA, Spinazzola J, Blaustein ME, et al: A randomized clinical trial of eye movement desensitization and reprocessing (EMDR), fluoxetine, and pill placebo in the treatment of posttraumatic stress disorder: treatment effects and long-term maintenance. J Clin Psychiatry 2007; 68:37–46
10. Freud S: Mourning and melancholia, in The Standard Edition of the Complete Works of Sigmund Freud, vol 14. Edited by Strachey J (trans. ed.). London, Hogarth Press, 1975, pp 237–258
11. Buckman JEJ, Underwood A, Clarke K, et al: Risk factors for relapse and recurrence of depression in adults and how they operate: a four-phase systematic review and meta-synthesis. Clin Psychol Rev 2018; 64:13–38
12. Cuijpers P, Driessen E, Hollon SD, et al: The efficacy of non-directive supportive therapy for adult depression: a meta-analysis. Clin Psychol Rev 2012; 32:280–291
13. Ehlers A, Bisson J, Clark DM, et al: Do all psychological treatments really work the same in posttraumatic stress disorder? Clin Psychol Rev 2010; 30:269–276