Reviewer’s report

Title: Psychosocial functioning in patients with treatment-resistant depression after group cognitive behavioral therapy

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Reviewer: Yves Chaput

Reviewer’s report:

This article pursues some rather lofty goals. Indeed, the authors attempt to assess the effect of cognitive behavior therapy (administered in a group setting) on psychosocial functioning (or at least some aspects of psychosocial functioning) and on depressive symptoms (although this does not appear to be a primary goal), in patients with treatment refractory depression (TRD). The long-term follow-up aspect of this study is a very nice addition as it is something that is not often seen in the literature. Overall, this topic is of interest and worthy of publication. This study however has several shortcomings as well as some unclear sections that tend to reduce its readability and pertinence.

I will address these issues in both major compulsory revisions and minor compulsory revisions. Major revisions are those that the authors must consider answering and, if in disagreement with the point, then they should provide logic and evidence in support of their reasoning. Most all pertain to unclear, redundant or otherwise questionable logic and methodology within the manuscript. There are also several issues I have with regards the data itself.

Minor revisions are points are the authors could automatically without need for a response.

Discretionary revision points are those that I think might enhance the manuscript but are mere suggestions to the authors.

Major revision point 1;

I have some issue with the overall reasoning behind this study. The background section lacks focus (this may be due to the writing style of the manuscript though).

In the first paragraph the authors define TRD. In the second, they review articles suggesting a relationship between depressive symptom severity and poor psychosocial functioning. They conclude saying ‘Such results suggest that combining a psychosocial approach with drug therapy could be important in the management of TRD”. Does this imply that CBT may improve TRD by reducing poor psychosocial functioning, regardless of its effect on depressive symptoms or, alternatively, that CBT can improve TRD by reducing depressive symptoms and as a consequence, reduce psychosocial dysfunction? The third paragraph consists in a review of the efficacy of CBT in TRD (the Fava article being more
pertinent here, although it is an open trial. The Moore article is, from reading the abstract, a pilot study of a small number of patients receiving CT sequential to their antidepressant treatment. In this light, perhaps the authors should also consider the Thase study, which is similar but 10 years later, Am J Psychiatry, 2007, 164:739). Finally, the fourth paragraph is on chronic, but not necessarily TR depression. In the fifth, they state the goals of this study, elaborating only on social functioning and not at all on depressive symptomatology, although they collect such data throughout this study.

If the overall philosophy behind this study is....

....A- some patients are treatment refractory, defined by.... B- These patients, because of the sustained depressive symptoms, have reduced psychosocial functioning.... C- Some studies show that sequentially administering CBT to antidepressant therapy in TRD may be of benefit in reducing depressive symptoms… D- To date, few studies have examined the effect of the sequential administration of CBT in TRD on both depressive symptoms and psychosocial functioning… E- We intend to do just that...

.....then it should be clearly stated.

Major revision point 2;

One of the great advantages of online journals is the lack (within reason) of a space requirement. Word counts worries are part of the past and authors can concentrate on fully explaining their data. The authors of this study should take maximum advantage of this possibility. I will give a few examples of what I mean in several of the manuscript's sections.

First, the abstract does not fully reflect the content of this manuscript. In the methods subsection of the abstract the authors mention all rating instruments used. In the results section, data for only 2 of the 5 rating scales is given.

Second, in the methods section, care should be taken to fully document treatment refractoriness. Although I find it great that they are using a well-defined staging system for TRD, they still have to explain how they got there. They might include a paragraph (or table) stating the antidepressants used (at least the most frequently used ones), the dosages they consider to represent an adequate trial of each and, the duration of treatment. For instance, citalopram was taken at an average of 40 mg per day (range 30 to 60 mg, N=...), for a minimum of 8 weeks.

Third, again in the methods section, were any modifications of the current medication allowed in this study. Were there any concomitant drugs allowed in this study and / or did they vary in dose?

Fourth, in the results section, ranges should be given for the rating scale averages. For instance, for the HRSD and GAF scales, we should know what the ranges are. Given that the averages are, at best, modest, a distribution would be appropriate. For example, of the 38 patients, N=7 had HRSD between 9 and 14, N=20 had scores of between 15 and 18 and N=11 had scores 18 and above.....
Fifth, also in the results section, more detail should also be given for the HRDS end points. In table 3, it is stated that 55% of patients were in remission. However, it is much easier to be in remission if patients stated out the trial with a HRSD of, say, 9. The drop would be a scant 2 rating points. So in essence, patients could be in remission and not fulfill the criteria for 50% improvement here.

Sixth, again in the results section, the ever-dwindling number of patients on follow-up is simply not explained. We go from 38 at end point, to 28 without explanation (although the 28 to 20 drop is explained).

There are several other examples although at this point I will conclude this section.

Major revision point 3;

What was the justification for using such a low cut off point for the HRSD. I think there would be general agreement that patients with a HRSD score of 8 to 12 would be considered, at best, very mildly depressed. If patients entered into this study had a HRSD of 8 or 10 then how do the authors should explain this with regards their own entrance criteria (of stage II or greater depression)? Also, how do they explain this with regards their triage system (the SCID mentioned in the Methods section)?

Major revision point 4;

Why was group, rather than individual CBT chosen for this study? Although the jury is not at all definitive on this point it is possible that CBT in the individual setting be slightly more efficacious for depressive symptoms on the median term (6 months post treatment). Cost effectiveness is also debatable (Tucker, Beh Cog Psychotherapy 2007: 35:77).

Major revision point 5;

I also have an issue with how the authors are analyzing their data. We go from intent to treat (ITT) on 43 patients and end up with 20 at the 12-month follow-up. Statistics are only run on these latter. Statistics are only run on the 38 completers of the active phase of the study also. Where is the concept of LOCF here (last observation carried forward). Did the protocol not include a LOCF at the time of withdrawal from this study or were endpoint ratings only done on those who actually reached endpoint? If so, then the authors should be especially careful in their interpretation of their results. For instance, take the GAF scores at endpoint that increase from 60 to 67. Not a huge increase but again, it is clear that some of these patients are but very mildly depressed. The problem here is that N=38, so that the 5 drop outs are not included. As drop outs frequently do so due to lack of efficacy, then what would the inclusion of a 12% of reduced GAF scores have on this average (indeed, on all of the other averages of the other rating scales also)? Would the conclusions of this manuscript be the same? This may not be a huge problem for the active phase of the study if the response in the 38
patients is consistent, but it might be for the follow-up phase, where the drop out rate is much higher.

Major revision point 6;

Would a comparison group of TAU (treatment as usual) not have been warranted here, given the population studied and the modest level of psychopathology?

Major revision point 7;

I think there is a certain amount of confusion with regards reporting of the HRSD scores for the long-term portion of this study on page 14 (results section). They state that the HRSD scores at follow-up are higher than at baseline or at end of the active treatment. This would imply that patients are less well. This is not at all mentioned in the Discussion or Conclusion section, which is odd. In fact, on page 17 of the Discussion section active treatment gains are once again mentioned, but not the follow-up HRSD scores. Are we to assume that the authors made a typo in the results section and that the final HRSD scores are also maintained at a lower level?

If this is not the case then the authors have a bit of explaining to do.

Minor revision point 1;

The authors should correct some obvious typos, such as on page 3, in the phrase ….Group-CBT involved of 12 weekly… and also on page 9, where it is written …twelve 90-minite sessions… There are other examples.

Also, some phrases are just a bit difficult to understand largely due to sometimes odd word selections. For instance, the “development of pharmacological strategies in the treatment of major depressive disorder is remarkable” on page 5. Remarkable is perhaps not the most appropriate choice of words, although one gets the message.

Likewise, on page 15 in the Discussion section, the phrase beginning with “In the present study, these scores…”. This phrase is difficult to understand which is unfortunate as they are making an important point (contrasting their results with those of Dunner et al, one of the few comparable studies).

Another example is on page 16, in the phrase “It is possible that chronic depression in these studies might be involved with treatment –resistant…”. The choice of the word ‘involved’ here is difficult to understand and again, the authors are making an important point.

These things tend to distract the reader who is usually quite busy and may not take the time to re read a phrase or paragraph.

Discretionary revision point 1;

An abbreviations section at the end of the manuscript would be useful.

Discretionary revision point 2;
I would add the time line to the flow chart (ie, Entered group-CBT (day 1), Completed ...(day X).....

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests