Reviewer's report

Title: Neurocognitive profiles in treatment-resistant bipolar I and bipolar II disorder depression

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Reviewer: Corin Bourne

Reviewer's report:

Overview

The study’s aim was to investigate and compare the cognitive profiles of BDI & BDII patients (using the 9 tests within the 6 cognitive domains of the MCCB) in a current depressive episode (operationalised as MADRS score >= 25) and to explore the relationship between cognitive function and illness characteristics. The authors appropriately controlled for age and gender effects in their analysis. The paper reports data on 19 BDI and 32 BDII patients. Whilst these relatively low sample sizes are a limitation they are not surprising given the clinical status of the target population. This paper offers data on an under researched topic and greater knowledge in this area would clearly be valuable in improving quality of life for patients with BD. I therefore commend the authors for undertaking such work and feel that it has significant potential contribution to the literature.

Comments

As noted above, I commend the authors for undertaking research in this potentially valuable area. I believe the paper has a significant potential contribution to the literature and my suggestions (outlined below) are designed only to increase the clarity, flow, and impact of the current paper.

Abstract

1. In Results, the authors state that “impairments were evident in... all MCCB domains”. It would be interesting to consider the effect size of these impairments against patients with similar symptoms levels within unipolar depression. Whilst this comparison would sit best in the Discussion section, it may lead to the authors choosing to modify the statement in the Abstract e.g. “impairments were evident in... all MCCB domains over and above those found in unipolar patients with similar depression levels.” or “impairments were evident in... all MCCB domains comparable with those found in unipolar patients with similar depression levels.” Similarly, the authors state that “higher age was associated with greater... deficits compared to age-adjusted published norms.” Again, are these greater (or comparable) age-related deficits than a unipolar depression group?

2. In Conclusions, the authors state that “impairments were worse in BDI compared to BDII patients, particularly processing speed”. This statement clashes slightly with the early statement in Results that “significant difference [between BDI & BDII] on one of the measures, category fluency.” Whilst,
category fluency is one of the measures within the cognitive domain of processing speed, the performance of BDI & BDII is not significantly different overall on processing speed (Table 2). The authors should clarify that they are referring to percentage of patients within the groups that reach clinically significant levels of impairment (i.e. Table 3).

Results

3. Demographics. A sample with 48% benzodiazepine users seems quite high. Whilst I note that this sample is deliberately selected to have treatment-resistant depression and be current inpatients which may partly explain the relatively high level of benzodiazepine use, I am also aware that pharmacological prescribing practices are often culturally or nationally bound. It would be really helpful if the authors could add some commentary on how typical this Norwegian sample’s pharmacology is relative to other nationalities. I would also be slightly circumspect with regard to the findings of speed of processing given this level of benzodiazepine use.

4. Influence… cognitive functioning. The last sentence in this section “Diagnostic subtype BDI…” is a re-statement of the last sentence of the first paragraph of the “Neurocognotive profile” section. It would be better to delete the sentence from the current location and incorporate it into the earlier paragraph.

Discussion:

5. 1st para. “Almost half of the patients were impaired in two or more domains, indicating that cognitive deficits are frequent in BD depression.” I would be inclined to amend the end of this sentence to say “indicating that cognitive deficits are relatively common and non-specific in BD depression.”

6. 1st para. “Speed of processing was also found to be the most severely affected domain in studies involving BD patients in the euthymic phase [27, 45].” I find these references slightly odd (especially the older adults paper given this samples mean age). The authors may wish to cite the several meta-analyses that have been conducted on euthymic patients: Arts, Jabben, Krabbendam, and van Os (2007); Bora, Yucel, and Pantelis (2009); Robinson, Thompson, Gallagher, Goswami, Young, Ferrier, and Moore (2006); Kurtz and Gerraty (2009); Mann-Wrobel, Carreno, and Dickenson (2011); and Torres, Boudreau, and Yatham (2007). These papers tend to show that verbal learning and executive function are the most impaired domains suggesting that depression may have a particular extra effect on speed of processing (or indeed this may be an artefact of the high level of benzodiazepine use [see pont 3 above]).

7. 9th para. The authors acknowledge the limitation of their sample size. However, it would be helpful if this limitation was referred to as a possible explanation for lack of significant findings in several places e.g. 4th para on depression severity and impairment; and the lack of other illness associations (last para of Results section).

Conclusion:

8. The statement that “cognitive impairments were worse in BDI compared to
BDII patients, particularly processing speed.” is misleading (see point 2 above). Please rephrase.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.