Reviewer’s report

Title: Brain structural changes associated with antipsychotic treatment in schizophrenia as revealed by voxel-based morphometric MRI: an activation likelihood estimation meta-analysis

Version: 2 Date: 22 September 2013

Reviewer: Jennifer Robinson

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When assessing the work, please consider the following points:

1. Is the question posed by the authors well defined?

The question is well defined, and the area of interest is important. However, I do not know that the results are indicative of antipsychotic usage. There are several scientific and statistical issues that I have with this manuscript. First, if there are known prodromal structural deficits, how can you conclude that the results you are seeing in the meta-analysis (of which only a handful of studies are pre-post treatment effects) are not the result of pre-morbid structural deficits? Secondly, the mixing of typical and atypical could be problematic as they act on different neurotransmitter systems (which of course innervate different brain regions). Third, I don’t think there was a compelling argument for the surprising finding of volumetric excesses.

2. Are the methods appropriate and well described?

The methods are adequately described.

3. Are the data sound?

The data are as best as they can be with the current state of the literature, however, I think the conclusions are overstated given the heterogeneity of the search space. While one of the strengths of meta-analysis is to overcome this, that relies on having an adequate sample size (i.e., a large number of studies with similar contrasts). This study has a small number of studies, and within studies, there is significant variability both in type of antipsychotic examined, and groups studies (either pre-post within subject design or between subject designs).

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
As stated above, I think there is an adequate discussion regarding the volumetric decreases found in the studies, but hardly any discussion regarding the excesses, which warrants a greater discussion given that it goes against what the most popular theories are.

6. Are limitations of the work clearly stated?
To a degree, yes. However, I think there needs to be more discussion regarding the heterogeneity of the results. I would like to see additional ALEs run (maybe comparing atypical vs. typical, where possible; or comparing within vs. between designs), to minimize the concerns I have with the search space.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes.

8. Do the title and abstract accurately convey what has been found?
Yes.

9. Is the writing acceptable?
The content of the writing is acceptable, however, the manuscript could use a read through for minor grammatical/spelling errors.

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

Declaration of competing interests:
I declare that I have no competing interests