Reviewer’s report

Title: Low Prevalence of Lipid Metabolism Abnormalities in APOE ε2-genotype and Male Patients 60 years or older with Schizophrenia

Version: 1 Date: 20 Dec 2016

Reviewer: Debby W. -Tsuang,

Reviewer’s report:

BMC Psychiatry

Low prevalence lipid metabolism abnormalities in APOE ε2-genotype senile schizophrenia patients

Ban et al

Schizophrenia has been largely managed by atypical antipsychotics, which have been associated with metabolic syndromes. This study examined the association between APOE genotypes and metabolic parameters in 294 schizophrenia patients (age 60 to 92) who had been chronically treated with antipsychotics. The authors found that patients with the e2 genotype had lower low-density lipoprotein and serum cholesterol levels than patients with the other genotypes. The authors conclude that elderly patients with schizophrenia and the APOE e2 genotype may be less likely to develop lipid metabolism abnormalities.

Strengths:

This is a relatively large study that concentrates on the Han Chinese population and investigates an interesting clinical question related to the side effects associated with atypical antipsychotic use in schizophrenia.

The findings from this study may enable future researchers to better tailor antipsychotic treatments for individual patients with schizophrenia. However, given that the clinical relevance of these findings is specifically for e2 carriers and that the e2 allele frequency is so low (i.e., 8% in this population), few subjects may actually benefit from these potential developments.

Weaknesses:

This manuscript would benefit from a statistical review. In particular, is it optimal to include each APOE allele as a separate independent variable (versus having one variable with three levels - e2/e3/e4)? The inclusion of so many independent variables may decrease the authors' power to detect differences.
It is also unclear to this reviewer why the authors divided the APOE genotypes into 3 groups. I am specifically concerned that the e3/e4 individuals were grouped together with the e4 homozygotes. Biochemically, these two groups likely differ.

In the discussion section, the authors should address survival bias, as these subjects are all over the age of 60. Is it possible that schizophrenia patients with severe hyperlipidemia would not have survived to be included in this sample?

The discussion section should also address whether the effects of these antipsychotics on metabolic syndrome differ according to duration of exposure. In other words, if metabolic syndrome were to occur in an individual undergoing treatment, would it occur within the first year of atypical antipsychotic treatment? Or can it occur much later? Is there a gender difference in this temporal effect? Discussing these matters would help to underscore the significance of studying elderly patients who have been chronically exposed to atypical antipsychotic medications.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:
1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal