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:** 14 Apr 2017

**Reviewer:** Alena Buretić-Tožmanović

**Reviewer’s report:**

It is an interesting study investigating glucose and lipid metabolism abnormalities in senile elderly schizophrenia patients.

The authors should make several changes in the text in order to improve the manuscript and put their results into context.

1. **Page 2, line 23:** this study is not testing the effects of long term antipsychotic use in schizophrenia patients because there are no control data of elderly persons not taking antipsychotic medication (authors could possibly refer to their recent paper in PLOS One, 2016 and could reconsider main aim of the study.

2. **Page 3, line 62:** One study found... (there are three references at the end of the sentence.

3. **Page 4, lines 63-72:** In general, this section is not clear enough. It would be better to present results of different studies in the Table showing the sample size, ethnicity, age, diagnoses etc. and the final results whether a connection between serum indicators and ApoE genotype was found or not.

4. **Page 5, line 88-92:** this text is unnecessary if the authors keep Figure 1.

5. **Page 7, line 138:** ApoE ε2/ε4 genotypes were excluded from the analysis; why is it not interesting for authors to measure serum markers associated with this particular genotype?

6. **Page 8, lines 154-158:** text is redundant since all the data were shown in the Figure 2.

7. **Page 8, line 169 - Page 9, line 184:** Why did the authors show the same results twice? I suggest to merge Figures 3 and 4 into one figure, and also to merge two paragraphs into one. Alternatively, the authors could keep Figure 3 only, stating no significant differences between ApoE ε3 and ApoE ε4 groups for other markers.
9. Regression analysis and Table 4.: the authors should present R, R2 (or Adjusted R2), F and P for each independent factor since their contribution is cumulative. Given results should be explained in the text more precisely. Why is regression analysis performed for triglycerides, and not for glucose or HDL serum level (should be explained)?

10. Table S1.: the authors should decide between Table 4 and Table S1 (which regression analysis is more informative or more appropriate).

11. Page 10, line 201: high blood pressure (definition is needed).

12. I do not find mean values for serum markers (total cholesterol, LDL cholesterol) for categories: male and female patients, atypical and typical antipsychotic medication, lipid-lowering medication and non lipid-lowering medication (see also 7.). Furthermore, it would be interesting to test combined effects: ApoE ε2+ X gender, ApoE ε2+ X atypical antipsychotic use etc.

13. Page 11, line 219: instead „...with ε2 alleles were relatively low.." write „...with ε2 alleles were significantly lower..."

14. Page 11, line 220: instead „...these value were high in patients..." write „...were significantly higher..."

15. Page 11, lines 226-227: where can the reader find the mean values of cholesterol and LDL cholesterol in patients taking and not taking atypical antipsychotics? The given statement should be documented.

16. Page 11, lines 230-232: „Therefore, we speculate...“ - the hypothesis should be placed in the Introduction section.

17. Page 12, line 234-237: to investigate possible gender effect is one of the goals; it should be emphasized among aims of the study.

18. Page 12, lines 239-245: this paragraph suits better for the Introduction section when the research problem is explained.

19. Page 12, lines 246-247: „... in previous studies. Only one study is cited. Check whether meta analyses exist on this topic or not.

20. Pages 12-13, lines 253-258: here I see the potential to compare previously published and present results (both groups present elderly population).

21. Page 13, lines 264-268: here, the authors summarize my main points but without addressing these issues I do not find relevant scientific result in their manuscript. I think that stated limitations could be easily eliminated.
22. Page 13, lines 271-276: Tables 4 and S1 inform us about possible protective role of the presence of ApoEε2 but the effect size which seems to be relatively small should be emphasized.

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.

No

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

No

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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