Comments on manuscript no.: 65951 Title: Lowered paraoxonase 1 activities may explain the comorbidities between temporal lobe epilepsy or mesial temporal sclerosis and depression, anxiety and psychosis. The above manuscript is very well written and will help in understanding pathological link between temporal lobe epilepsy and psychiatric conditions. I have some comments

1. Regarding various regression/multivariate analyses number of samples appears low. For examples, n=27 without comorbidities, n = 25 for mood disorders, n = 25 for psychosis etc.

@ANSWER: as shown in the tables and in the results section, regressions were performed in the total study group. This was stated in the text and can be deduced from the df values in the tables.

2. The total number of patients mentioned in the abstract is 104, while in the results section on page 13, first para, the number of sum of patients on various drugs is >300. If this is a case of polypharmacy then how the correlation can be made by comparing drugs individually

@ANSWER: this is now addressed in the text as:

These drug state variables were examined as dummy variables entered altogether in multivariate GLM analysis or one by one in univariate GLM analyses. However, both types of GLM analyses showed no significant effects of these drugs even without p-correction for multiple testing.

3. The word 'lowered' should be replaced with 'reduced'

@ANSWER: We have changed lowered into reduced all over the text.

4. Please mentioned nutritional factors and names of some chemicals in tobacco, which may induce seizures (page 17, 2nd para, last line). Is it nicotine or something else?

@ANSWER: this is now discussed in the text (discussion) as:

Nutritional factors which may affect PON1 activity include polyphenols, oleic acid, a Mediterranean diet, chokeberry and pomegranate juice, lipids, vitamin C and A [25].

And:

Harmful and potentially harmful constituents in tobacco that may trigger seizures are carbon monoxide, toluene, cresol, arsenic, acetone, ammonia, lead, and hexane [46].

5. Did the authors find any effect of low PON1 activity on cognitive functions, as has been reported by others.

@ANSWER: This was already addressed in the paper. Indeed, we reported on MMSE and that PON1 is positively associated with MMSE (see tables 1 and 5).

6. The authors should explain if they found any effect of the duration of treatment with AEDs or antipsychotics on PON1 and arylesterase activity.

@ANSWER: This study did not register the duration of treatment with AEDs, but registered type, dosage and total number of AEDS. This is now addressed in the limitations as:

Nevertheless, in the present study we did not control for duration of treatment with AEDs or antipsychotics on PON1 activities.

We hope that the paper is now in acceptable format,

Kind regards,

Prof. Dr. Michael Maes, M.D., Ph.D.