Reviewer's report

Title: Antibodies against phosphorylcholine are not altered in plasma of patients with Alzheimer's disease

Version: 1 Date: 27 June 2014

Reviewer: Julia Muenchhoff

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Silajdžić et al measured levels of anti-PC in plasma from 125 patients with AD, 176 control subjects, 19 patients with VaD, and 63 patients with other types of dementia. The anti-PC levels were not found to differ between these groups.

The manuscript is generally well written and easy to understand. The study aimed to replicate a previous report on different serum anti-PC levels in AD patients compared to controls, but no significant association was found here. As such, the study reports a negative result, which is often considered not publishable. However, replication of findings relating to biomarker discovery in independent cohorts is crucial and results failing to replicate other studies should be reported. The authors clearly and concisely report their findings without overstating their results. But the manuscript could be improved by adding more detail and revisiting the statistical analysis of the data.

Major compulsory revisions:

1. The statistical analysis seems quite basic. Please consider the following suggestions:
   a. If any additional relevant information such as ApoE #4 allele status were available for the participants, it should be incorporated into the linear regression analysis.
   b. Line 12, page 5 states that regression analyses were only carried out on all clinical groups. The analysis should also be performed on the control group to assess potential associations with MMSE, age, gender, etc within this group.
   c. Please give details of the variables CSF/serum albumin ratio, Aβ42, total tau and phosphorylated tau (mentioned in lines 12-15, p. 5) used for correlation in Table 1. Please explain how these were measured or provide reference if these data were published previously.

2. Please provide sample numbers for each of the “other” dementia types either within the brackets in line 18, p. 5, or in Table 1. Were plasma levels of anti-PC compared across these different types? Grouping them together into one “other dementia” group could obscure potential differences in anti-PC levels between these types of dementia.

3. The discussion of why the results from Eriksson et al 2010 did not replicate in this study (lines 6-11, p 7) should be expanded. What are the differences and
limitations of the study here and Eriksson et al 2010? Could the different type of
sample (plasma vs serum) or other factors such as fasting/non-fasting play a
role? What about other technical issues besides the type of assay, such as
sample preparation, storage, freeze thaw cycles, person performing the assay
etc? Line 11, p 7: either be more specific or delete the “laboratories”, as currently
this is contradictory to line 7, p. 7 “not due to differences in laboratory technique”.
Also, the same kit was used but presumably by different operators so there could
be differences in laboratory technique. It would be more accurate to say that
there are no differences in kit manufacture.

4. In methods paragraph “analysis of plasma anti-PC” (line 3, p. 5), please
provide more detail on the CVDefine assay used to quantitate anti-PC, such as a
very brief overview of assay principle and method including amount of plasma
required, the limit of detection, the CV etc. This information is still of interest here
even though it was published previously.

Minor essential revisions

1. There is a relatively small number of samples in the VaD group. Please state
the power calculation used in the study design or how the number of samples for
all groups was arrived at?

2. What does the asterisk in Figure 1 above control group represent? Please
explain in the figure legend.

3. Please rephrase the sentence starting in line 18, p.3.

4. Please include CVD in the list of abbreviations.

Discretionary revisions

1. Was a sensitivity test (exclude outliers and rerun ANOVA) performed to ensure
the outliers do not affect the outcome? From the box plot in Figure 1, this seems
highly unlikely as the number of outliers in control and AD group is very small
compared to the number of samples, but the authors might still want to check for
peace of mind.

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.