Author’s response to reviews

Title: The performance of rapid plasma reagin (RPR) titer in HIV-negative general paresis after neurosyphilis therapy

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Dear editor and reviewers: Firstly, thank you for your comments. According to your comments, I want to do some replies. And we have revised the changes in the manuscript by highlighting with red words. Editor Comments: Please correct your manuscript for spelling and grammatical errors. Answer: Many thanks for your comment. We have carefully corrected the grammatical errors and polished the writing again. It should be more readable and more scientific. We sincerely hope that the revision is satisfactory. Reviewer reports: Tim Read (Reviewer 1): Thanks for taking the time and going to considerable effort to revise your paper. I accept that your patient population probably all have neurosyphilis and that you have an adequate case-definition, although I wonder how confidently you can exclude Alzheimer's disease with coincident positive syphilis serology and a slight abnormality in protein or WBC in the CSF? If this is a possibility you may wish to mention it in your limitations paragraph. Answer: Many thanks for your comments. Parts of symptoms between GP and AD are similar. However there are several points which could use for differential diagnosis: 1) The symptoms of GP can be divided into early forms and late forms. Early symptoms include forgetfulness, personality changes, mood changes, headache, and changes in sleep habits. After a period of time, psychiatric manifestations, such as depression, hallucinations, delusions, or mania, will be generally developed. Worsening impaired memory and cognition can also be found during this period. However, cognitive impairment, which is the
leading manifestation of AD, usually occurs in the early stage and last for the whole stage of disease. 2) GP patients might have more complaints and positive signs in the nervous system than AD patients. What’s more, the symptom of patients with GP had improved after penicillin treatment, whereas the cognitive impairment of AD patients is slow but progressive. Ghanem KG. REVIEW: Neurosyphilis: A historical perspective and review. CNS Neurosci Ther 2010; 16: e157-168. Wang J, Guo Q, Zhou P, Zhang J, Zhao Q, Hong Z. Cognitive impairment in mild general paresis of the insane: AD-like pattern. Dement Geriatr Cogn Disord. 2011; 31(4):284-90. The English is awkward but can mostly be understood. I've made some suggestions for minor improvements:

Abstract: MMSE needs to be defined at first use.

Answer: Many thanks for your suggestion. We have defined MMSE at first use.

Lines 17 to 20. This is poorly written, very confusing and needs editing for fluency.

Answer: Many thanks for your comment. We have rewritten the sentence in the revised manuscript.

Background. Line 14. Delete "which is" (criteria is plural).

Answer: Many thanks for your suggestion. We have deleted "which is" in the revised manuscript according to your suggestion.

Line 21. State whether you mean CSF or serum RPR titre or both.

Answer: Many thanks for your suggestion. We have changed it in the revised manuscript according to your suggestion.

Methods. I think the hyphen between CSF-RPR is confusing as it resembles a negative sign. I suggest you delete it and use CSF RPR- and CSF RPR+.

Answer: Many thanks for your suggestion. We have changed it in the revised manuscript according to your suggestion.

P. 6 line 7. Delete the speech marks.

Answer: Many thanks for your suggestion. We have deleted the speech marks in the revised manuscript.

Results. P 8. Lines 1-5. As in the abstract it takes a lot of effort to understand what you're saying here. The phrase "the response to 4-fold decline in" is confusing. I think you mean this: In CSF RPR+ patients, the CSF RPR titre declined four-fold in 85% (11/13) and the serum RPR declined four-fold in only 46% (6/13), odds ratio 6.4 (95% confidence interval 1-41.2).

Answer: Many thanks for your suggestion. We have changed it in the revised manuscript according to your suggestion.

Hanna Jarva (Reviewer 2): The aim was to test whether RPR titer could be used in follow-up of neurosyphilis patients. Does this mean serum RPR or CSF RPR? I understand that this means serum RPR but this should be clarified. Furthermore, it is still unclear in several places whether RPR titer refers to serum titer or CSF titer.

Answer: Many thanks for your comments. We have clarified the expressions in the revision. Some of the limitations of this study are listed but their influence on the results is not discussed. The limitations should be taken into account when drawing conclusions.

Answer: Many thanks for your suggestions. We have mentioned it in the conclusions.

Discussion, p. 9, lines 18-21: these sentences are practically copied from my comment. Please, reformulate in your own words.

Answer: Many thanks for your comments. We have reformulated these sentences in our own words. There are numerous language errors. The language must be checked.

Answer: Many thanks for your suggestions. We have carefully corrected the grammatical errors and polished the writing again. It should be more readable and more scientific. We sincerely hope that the revision is satisfactory. Best regards

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