Author’s response to reviews

Title: Association of the MMP-9 polymorphism and ischemic stroke risk in southern Chinese Han population

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Dear Editors and Reviewrs:

Thank you for letter and for the reviewers’ comments concerning our manuscript entitled “Association of the MMP-9 polymorphism and ischemic stroke risk in southern Chinese Han population” (ID: NURL-D-18-00613). Those comments are all valuable and helpful for revising and improving our paper, as well as the important guiding significance to our researcher. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer’s comments are as flowing:

Responds to the reviewer’s comments:

Reviewer 1 (Leah Wormack, M.S.):

1. Response to comment:

The background poses and interesting setting for the necessity of the research. It elaborates well on research previously done in this field. The description of the relationship between MMP9 and ischemic stroke was briefly described. I believe the background/introduction would benefit from clear statement of the hypothesis that this manuscript is attempting to prove and what are
the clinical implications. Such as, what would the determination of MMP9 gene association with risk of ischemic stroke mean for the Han Population?

Additionally, the reader would benefit from some discussion of why these four SNPs (please define) were chosen, in the introduction.

Response:

1: The purpose of this study is to determine if susceptible single nucleotide polymorphisms (SNPs) in the MMP9 gene are associated with increased risk of IS in a southern Chinese Han population. These results may contribute to further clarify their potential role in IS and provide basis for the early prevention and targeted treatment of IS in a southern Chinese Han population.

2: Thank you very much for your question. In the method part of the manuscript, I added the reasons for choosing these four SNP sites. (In our study, four SNPs rs3787268, rs3918249, rs2274755 and rs3918254 in MMP-9 were selected for genotyping. Based on the research, it is found that rs3787268 has no correlation with IS in the Polish population, but it will increase the risk of IS in the western Guangdong region, indicating that the correlation between this site and IS is different in different populations, and it is still different. It is unclear whether the MMP-9 polymorphism is significantly associated with the is risk of the southern Chinese Han population, so it was chosen. The choice of rs3918249, rs2274755 and rs3918254 based on their effects on ischemic stroke has not been studied.)

Response to comment 2and 3:

Method

The strength of the methodology was that there was a direct control population for comparison. There was a clearly described selection criteria for the study participants which fits the aim of the study well. A systemic error in the methodology is that the control group was in no way matched to the participants, in age, gender, or other demographic factors, which invites in possible environmental variation.

Results

The results again make clear the systemic error in the methodology as the median age of the controls was 48.31 and the median age of the cases was 64.13, it is unclear what role this may play. However, the manuscript does identify that there is no statistically significant difference in the distribution of age and sex between cases and healthy controls.

Response:
Thank you very much for the question raised by the editor. However, due to the difficulty in collecting samples and the limitation of sample size, although our data analysis method is quite mature, this problem may be inevitable. In the future, we will continue to collect relevant samples for verification in a larger number of people.

Response to comment 5:

Discussion

The discussion includes a captivating rhetoric of why these particular SNPs were of interest to study. The discussion touched on all the limitations that this reviewer was concerned about in the study, i.e. sample size, limited to the Han population and not generalizable, lack of acknowledgement of other risk factors for ischemic stroke in the subject population.

Response:

Thank you very much for the question you raised. This paper IS only a basic study with certain limitations, but it also has positive significance. In the future, we will continue to study other risk factors of IS in depth

Response to comment 6:

Conclusion

Please add a conclusion subheading, for congruent formatting throughout manuscript, as well as have clear and concise wrap-up of the aims of this study and future work.

Response:

Conclusions have been added to the revised manuscript and marked in red.

Reviewer 2: (deren wang )

Response to comment 1:

The introduction section should be rewritten due to poor organization. Reading through the introduction, I could not understand why the authors choose the four SNPs of the MMP9 genes to study. That was also not stated clearly in the method section. In addition, the authors should be cautious to summarize the stroke ranking in China or the whole world. Please don't referencing data only from the report in upper Egypt(desert area), while this paper focused on data from China.

Response:
Thank you very much for your question. I have rewritten the introduction. In the method part of the revised manuscript, I added the reasons for selecting these four SNP sites.

Response to comment 2:

The inclusion and exclusion criteria should be refined and stated very clearly. Do the participants have some comorbidities such as hypertension, diabetes, etc.? The table 1 should also give other information such as clinical characteristics of the participants.

Response:

The inclusion and exclusion criteria have been refined in the revised manuscript. However, I am very sorry that because the samples were not easy to collect at that time, the clinical characteristics of the participants were not complete, so other clinical characteristics of all the participants could not be compared for analysis.

Response to comment 3:

The authors should also state clearly in the method section that the procedures of blood sampling. For example, what time point the blood was taken from the patients after stroke onset? How the blood was stored and transferred.

Response:

Thank you very much for your question. It has been revised in the method part of the manuscript.

Response to comment 4:

The language of the whole manuscript is indeed poor and needs to be improved! For example, the first sentence in methods section of the abstract "this study was including", the last sentence in that part "calculated for unconditional logistic-regression analysis", the first paragraph of the introduction "ischemic stroke is the most common accounted for", the second paragraph of the study participants "patients with ischemic stroke excluded those with". There are many other similar problems. Please check carefully through all the manuscript.

Response:

Thank you very much for your question. All the grammar problems in the manuscript have been revised in detail. We tried our best to improve the manuscript and made some changes in the manuscript. These change will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editor/Reviewers’ warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.
Thank you and best regards.

Yours sincerely,

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