Author’s response to reviews

Title: Genetic Polymorphisms of Nerve Growth Factor Receptor (NGFR) and the Risk of Alzheimer’s Disease

Authors:

Hui-Chi Cheng (aishchi@gmail.com)
Yu Sun (sunnyu.ji.lu@gmail.com)
Liang-Chuan Lai (llai@ntu.edu.tw)
Shih-Yuan Chen (bytegene@gmail.com)
Wen-Chung Lee (wenchung@ntu.edu.tw)
Jen-Hau Chen (jhhchen@ntu.edu.tw)
Ta-Fu Chen (chentf@ms4.hinet.net)
Hua-Hsiang Chen (tn607732@gmail.com)
Li-Li Wen (eckwen@yahoo.com)
Ping-Keung Yip (liuyip@ms23.hinet.net)
Yi-Min Chu (juimin2003@yahoo.com.tw)
Wei J. Chen (wichen@ntu.edu.tw)
Yen-Ching Chen (karenchen@ntu.edu.tw)

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Author’s response to reviews: see over
Dear Professor Olsen:

Attached please find our response to reviewers’ comments on our manuscript MS: 8160478136315307 “Genetic Polymorphisms of Nerve Growth Factor Receptor (NGFR) and the Risk of Alzheimer’s Disease”, which was submitted to Journal of Negative Results in Biomedicine as a research article.

We have responded to the reviewers’ comments in detail. We look forward to your decision; please let us know if we can provide any further information or details of the study.

Sincerely,

Yen-Ching (Karen) Chen, ScD
Assistant professor
Institute of Epidemiology and Preventive Medicine
Department of Public Health
Research Center for Gene, Environment and Human Health
College of Public Health
National Taiwan University
E-mail: karenchen@ntu.edu.tw
Reviewer's report
Title: Genetic Polymorphisms of Nerve Growth Factor Receptor (NGFR) and the Risk of Alzheimer's Disease (MS: 8160478136315307)
Version 1 Date: 3 December 2011
Reviewer number: 1

Major points
1) The two populations are not age-matched. Controls are younger than patients, implying they could develop the disease in the future (i.e. when they will reach patients’ age). Age ranges should be the same for the two populations, and analysis should be re-run excluding youngest controls. In addition, were controls tested for cognitive impairment? Were MMSE scores available?

Response: a) This is an important point. We consistently excluded both cases and controls whose age were less than 60 years old. To solve the issue of age difference between cases and controls, we then did a “frequency matching” with a 5-year interval to control for age difference between cases and controls. Conditional logistic regression model was used to re-do all the statistical analyses. After exclusion of participants with age<60 and use of frequency matching, the main effects showed minor change in both magnitude of effect (odds ratio) and significance remain the same. For subgroup analyses by type 2 DM, the association observed for rs2072446 and Hap1 remained quite the same (Table 5 and Table 6). b) Controls were recruited from health checkup and Short Portable Mental Status Questionnaire (SPMSQ) was used to assess controls’ cognition.

2) Results: considering that ten patients only have EOAD, last paragraph could be deleted.

Response: We have deleted the last paragraph of RESULTS. In addition, we deleted participants aged<60 (EOAD) and keep only LOAD (age>=60) to prevent confusion. All analyses were re-do based on LOAD and age-matched (frequency matching) controls.

3) Discussion need a careful revision regarding two points: a) first paragraph, last sentences: delete considerations about LD, that are basic concepts, b) third paragraph: the association observed could not necessarily be due to rs734194. It is possible that other rare polymorphisms not analyzed here are responsible for the association observed.

Response: a) The last sentence of the 1st paragraph in Discussion has been deleted per reviewer’s suggestion. b) This is an important point and we have included this information (rare polymorphisms) into the 3rd paragraph of Discussion and revise the sentence accordingly.
4) Figure 2 can be deleted.

Response: Figure 2 has been deleted per reviewer’s suggestion.

5) Lastly, language needs a careful check (i.e. “strong LD” instead of “highly LD”; “under the assumption of an additive model” instead of “under the additive model”).

Response: The modification has been made for “strong LD” (last sentence, 1st paragraph of DISCUSSION). In addition, three corrections have been made for “under the assumption of an additive or dominant model” (last paragraph of METHOD, 3rd and 4th paragraph of RESULTS).