Author's response to reviews

Title: No relationship between 2',3'-cyclic nucleotide 3'-phosphodiesterase and schizophrenia in the Chinese Han population: an expression study and meta-analysis

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Version: 3 Date: 12 March 2009

Author's response to reviews: see over
March 12, 2009

Dear the Editor,

I would be grateful if you could kindly consider to have our revised manuscript of “No relationship between 2’,3’-cyclic nucleotide 3’-phosphodiesterase and schizophrenia in the Chinese Han population: an expression study and meta-analysis” published in the category of regular research article in your journal. There is no financial interest. And I have the permission giving by all the authors. All the consent of patient in form of a signature can be received of a recognizable patient and kept by us. We would like to declare that this manuscript has not been, and will not be submitted elsewhere for publication before the decision made by you.

We look forward to hearing from you soon.

Yours sincerely,

[Signature]
The following are the response to reviewers and editor’s comments.

Version: 2 Date: 4 March 2009  
Reviewer: Esa Veli Juhani Leinonen  
Reviewer's report:  
1-On my mind a limitation: "no structural diagnostic interview method was used" should be mentioned in chapter "Subjects".  

Answer: Thank you for your suggestion. I add this limitation "No structural diagnostic interview method was used." in chapter "Subjects".

2-also that "patients were selected to antipsychotics according to clinical decision" should be stated.

Answer: As you suggest, I state in chapter "Subjects": "All patients were subjected to a washout period of more than eight weeks and then treated with a single antipsychotic chosen according to individual clinical assessment as follows: …"

3-Although promised in the answer of authors, the 5 SNPs are not given in the text in chapter "genotyping".

Answer: As you suggest, I state in chapter "genotyping": "For SNP selection, we used the HapMap database (www.hapmap.org) and included five SNPs (rs4796750, rs8078650, rs2070106, rs11079028 and rs4796751) from the Chinese section."

Version: 2 Date: 28 February 2009  
Reviewer: Albert Wong  
Reviewer's report:

The authors have substantially modified the manuscript and have addressed my previous comments. The writing still requires improvement, and is of variable quality throughout. Informal vernacular is mixed with formal academic style.

Answer: Thank you for your kind suggestion. I corrected the language as the following.

1 In the Abstract Method: Five CNP single nucleotide polymorphisms (SNPs) were investigated in a
Chinese Han schizophrenia case-control sample set (n=180) using direct sequencing. The results were included in the following meta-analysis.

2 In the Abstract Result: Our meta-analysis produced similar negative results.

3 In the Background: Tkachev et al. found that the brains of schizophrenia and bipolar patients showed down-regulation of key oligodendrocyte and myelination genes, as well as of transcription factors that regulate these genes, compared with control brains.

4 In the Background: CNP maps to 17q21.2, a region which shows strong evidence for linkage with schizophrenia as indicated by a study in a single pedigree.

5 In the Background: A number of studies have recently been carried out on transgenic mice to clarify the role of CNP.

6 In the Methods Subjects: Those identified as schizophrenia patients were then diagnosed for inclusion in subgroups as follows: …

7 In the Results: Some results were discarded on the basis of showing deviation after four replications. We obtained valid expression data for 79 schizophrenics and 84 controls. As shown in Fig 2a, the expression of CNP was reduced by 10% in the 79 schizophrenics compared with the 84 controls, but the difference was not significant.

8 In the Results: Fig 2e shows the effects on the expression of CNP of the four antipsychotics used …

9 In the Results: Previous reports on schizophrenia have suggested that…

10 In the Results: Our results suggest that expression levels of CNP in schizophrenic patients are lower by only 10% compared to unaffected controls, an insignificant difference.

11 In the Results: To date, no publication has reported the effect on CNP expression based on different schizophrenic subtypes and different drug treatments. Our data showed no statistically significant differences with respect to two major diagnosis subtypes and the four antipsychotic-treating subgroups. However, we need to be cautious in drawing this conclusion because the sample size is relatively small. The different gender distribution between patients and controls also presents a potential complication.

12 In the Conclusions: To sum up, our expression assay did not support a relationship between CNP and schizophrenia in the Chinese population.

13 In the Conclusions: Ethnic background is a factor to be considered in further functional research on oligodendrocyte- and myelin-related pathways and their roles in the pathology and etiology of psychiatric disorders.