

Response to the reviewers

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: Dear authors, I have a few comments on your manuscript: -

1. Introduction: You write that the etiology of PD is complex. Which etiological factors contribute to the development of PD?

Author: Thank for your suggestion, we have changed the sentence in the introduction section into: 'However, the etiology of PD is multifactorial and complex, involving genetic, environmental, psychological and neurobiological factors [2,3].'

2. As of genetic factors, how much of heritability is estimated in PD?

Author: We have changed the sentence in the introduction section into: 'Recent studies examining twins and family shows that the heritability of panic disorder is 30-40%, suggesting strong evidence for a genetic etiology.'

3. Are there any genome-wide association studies on PD, with which results?

Author: Yes, there is a GWAS study, the largest one so far, comprising 2248 PD patients and 7992 matched controls originated from four European countries. However, no genome-wide significant locus was identified (PMID: 31712720). Another GWAS of 1314 PD patients and 1127 controls from Germany also did not find any significant associations (PMID: 21655053).

4. Apart from the GAD1, which other genes are important in the PD's etiology?

Author: Yes, there are some other genes that have been suggested to be important in the PD's etiology. We have changed the sentence into: 'To date, genetic studies have reported several susceptibility genes for PD such as NPY (neuropeptide Y), COMT (catechol-O-methyltransferase) and particularly 5-HT system-related genes [5,6].'

5. Introduction: Which hypotheses did you test?

Author: In the last paragraph of section one, we have changed the sentence into: 'to test the hypothesis that the GAD1 polymorphism could be associated with PD, we have conducted a case-control study comparing the frequency of these SNPs (rs1978340 and rs3749034) in PD patients and healthy controls. Additionally, we examined the relationship between the presence of PD symptoms and these polymorphisms.'

6. - Methods: Was the number of PD patients a healthy controls sufficient to prove the effect of the GAD1 gene polymorphisms?

Author: Yes. We looked up the polymorphism frequency from the 1000 genome website as the control group and looked up the polymorphism frequency in psychiatric disorder patients from a study let by Stefano Marengo 'Genetic Modulation of GABA Levels in the Anterior Cingulate Cortex by GAD1 and COMT'. We used an online tool (<http://powerandsamplesize.com/Calculators/Test-Odds-Ratio/Equality> for sample size evaluation.) to calculate the sample size, set the desired statistic power as 0.7, and Type I error rate, $\alpha = 5\%$ to get the estimated sample size of 230.

7. Did you perform the statistical power analysis before the study?

Author: Yes, before the study, we have looked up the frequency of the polymorphisms from the 1000 Genome website (<https://www.internationalgenome.org/>) (For rs1978340 and rs3749034 are 0.2 and 0.15 respectively). For the frequency in psychiatric disorder group, as we used the information from study let by Stefano Marengo 'Genetic Modulation of GABA Levels in the Anterior Cingulate Cortex by GAD1 and COMT' (For rs1978340 is 0.30, for rs3749034 is 0.24), and used the online calculator <http://powerandsamplesize.com/Calculators/Test-Odds-Ratio/Equality> for sample size evaluation. We set the desired power of the study is 0.7, and the Type I error rate, $\alpha = 5\%$, case:control ratio is 1, the calculator gives the results is 230, which is approximately the sample size of our study.

8. - Results: Would you state more clearly what you mean under the terms "urban location" and "rural location"? The definition of these locations may be different in different parts of the world.

Author: a general way to define the 'urban location' and 'rural location' is based on the population size and density of the areas. In China, we define our patients' location based on their 'Hu Kou Ben' (Household registration booklet) which shows you belong to urban area or rural area)

9. Table 2: The title is not correct, because the table involves not only PD

patients but also controls. - At several parts of your manuscript, especially in the tables, you write "polimorphisms" instead of "polymorphisms".

Author: Thank you for your comments. we have revised the titles for Table 2 into "Table 2. GAD1 gene polymorphisms of patients with PD versus controls in the Chinese population" and also corrected the typo.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is an excellent work both in terms of scientific quality and in terms of the presentation and classification of the results. The style and language of the manuscript are brilliant. The results are of high relevance, especially since a Chinese sample was examined here. In my opinion, the work meets the high standards of the World Journal of Psychiatry and can be recommended for publication.

10. - A small suggestion for improvement: the heading for Table 2 should read: "GAD1 gene polymorphisms of patients with PD in this Chinese population"

Author: Thank you for your suggestion, we have corrected the title into: 'Table 2. GAD1 gene polymorphisms of patients with PD versus controls in the Chinese population'