

Reviewer Comments:

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Dear authors, I have several comments on your manuscript: - In Abstract, you use the abbreviation CATM, which is not explained.

Answer: Thank you so much for your positive comments. This is a very important point raised by the reviewer. We have added the following contents to the Abstract in AIM : “chronic antipsychotic-treated male (CATM)”

- In Abstract - Methods, you write about "neuropsychological tests", this should be specified more, which tests, what are they aimed at?

Answer: Thanks for the kind comments on quality improvement. We have added sentences in Abstract – Methods: “Neuropsychological tests, such as the Digit Cancellation Test (DCT), Semantic Verbal Fluency (SVF), Spatial Span Test (SS), Paced Auditory Serial Addition Test (PASAT), Trail Making Task (TMT-A), and Block Design Test (BDT), were used to assess executive functions (BDT), attention (DCT, TMT-A), memory (SS, PASAT), and verbal proficiency (SVF).”

- In Abstract - Methods: You do not write that you examined BDNF, but BDNF is stated in the title of your manuscript.

Answer: This is a very important point raised by the reviewer. we have now corrected in Abstract - Methods: “The serum levels of follicle-stimulating hormone (FSH), and BDNF were compared between CATM patients with SCZ (n = 120) and healthy controls (n = 120).”

- You should explain whether the number of your study subjects was based on a statistical power analysis.

Answer: Thank you for your helpful suggestion. We have added sentences in the MATERIALS AND METHODS-Participants section: “This was a case-control study, and the sample size calculation method was as follows: $\alpha=0.05$, $\beta=0.20$, Meant=0.25, and Meanc=0.21; the sample size calculation was input into the Biostatistics website (www.cnstat.org/samplesize/12/), and the difference between the two sets of means was compared, n=200 (cases). If the maximum number of lost cases was considered to be 20%, then the total number of cases in both groups should be: $200+200 \cdot 0.2 \approx 240$ (cases), $n_t = 120$ (cases), $n_c = 120$ (cases), and power=0.8036.”

- The grammar in your article is good, but you sometimes use inadequate words. E.g., males are designated as "guys", some patients are designated as "weak people". The text should be revised by a native speaker of English who is experienced in psychiatric scientific writing.

Answer: Thank you very much for mentioning the error, which we have now corrected inadequate words. We thank MedE Editing Group (<http://meditorexpert.com>) for editing this manuscript.

- In the line No 220, I found some Chinese characters in the middle of the English text.

Answer: Thank you very much for mentioning the error. We have deleted the Chinese characters.

- In the line 239, you state that clozapine is a new antipsychotic, but clozapine was synthesized in 1958. The reviewer

Answer: Thank you very much for mentioning the error, which we have now corrected inadequate words.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This study entitled "Brain-derived neurotrophic factor, sex hormones, and cognitive decline in male patients with schizophrenia taking continuous antipsychotic therapy" seems to have been generally well executed and written. Furthermore, I believe that this paper will be of great interest to the readers. However, I have only a few remarks that require authors' attention. Title Please add the type of article in your title.

Answer: Thank you so much for your positive comments. We have already added the type of article in the title.

Abstract Background Add this section in your Abstract, here, in one-two sentences describe the background of your study and more clearly describe the aim of your study. Objective section should be integrated with Background section. See previous comment.

Answer: This is an excellent point. We have added sentences in Abstract-BACKGROUND:

"There are systematic differences in clinical features between women and men with schizophrenia (SCZ). The regulation of sex hormones may play a potential role in abnormal neurodevelopment

in SCZ.” We have added sentences in Abstract–AIM: “The purpose of this study is to investigate whether the communication between BDNF and sex hormones is involved in the clinical symptoms and cognition of CATM SCZ patients.”

State the term in full when it is mentioned for the first time in text (e.g., BDNF, CATM).

Answer: We appreciate your good suggestions. Abbreviations be defined upon first appearance in the text.

Introduction Please state the clear hypothesis of your study at the end of Introduction.

Answer: We agree with the reviewer’s comment and have changed the sentence at the end of Introduction, “The relationships between sex hormones, BDNF, clinical symptoms, and cognitive function in CATM patients should benefit greatly from the findings.” to “We hypothesize that neurotrophic factors mediate cognitive decline in male patients with chronic schizophrenia via hormones.”

Methods In your first sentence add an information what type of study you have performed.

Answer: This is an excellent point. We have added sentences in Methods: “This was a case-control study, and.....”

Statistical Analysis Why the sample size calculation was not performed?

Answer: We agree with the reviewer’s comment and have added sentences in the MATERIALS AND METHODS-Participants: “This was a case-control study, and the sample size calculation method was as follows: $\alpha=0.05$, $\beta=0.20$, $Meant=0.25$, and $Meanc=0.21$; the sample size calculation was input into the Biostatistics website (www.cnstat.org/samplesize/12/), and the difference between the two sets of means was compared, $n=200$ (cases). If the maximum number of lost cases was considered to be 20%, then the total number of cases in both groups should be: $200+200 \cdot 0.2 \approx 240$ (cases), $nt = 120$ (cases), $nc = 120$ (cases), and $power=0.8036$.”

Results State exact P values, not just $P < 0.05$.

Answer: This is an excellent point. We have changed the sentence at the end of Introduction, “ $\alpha = 0.05$ ” to “The significance level was set at $P < 0.05$.”

Discussion. Please state the limitations of your study at the end of Discussion.

Answer: We appreciate your good suggestions. We have added sentences in the last paragraph of Discussion , “The limitations of this study require consideration. The lack of confirmation regarding is the primary limitation of this study.”