Author’s response to reviews

Title: The association between BDNF Val66Met polymorphism and emotional symptoms after mild traumatic brain injury

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Author’s response to reviews:

Dear Editor,

We are submitting a revised manuscript entitled “The association between BDNF Val66Met polymorphism and emotional symptoms after mild traumatic brain injury”. We would like to express our gratitude for both the reviewer’s scrupulous work and the positive comments about the suitability of publications at BMC Medical Genetics.
The reviewer identified some of our grammatical mistakes and give many valuable comments to improve the manuscript. We have revised the manuscript and point-by-point replied to each comment with blue color, to clarify the clarifications and improvements asked.

Finally, we would like to thank you for allowing us to submit a revised version of this manuscript, and hope that you would recognize that we have carefully updated our manuscript to address your concerns.

The authors have declared that no competing interests exist.

Sincerely yours,

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Leigh Christopher (Reviewer 1):

Grammar/spelling:

*pg 12 line 26-sixth week (not sixth weeks) throughout when talking about the results for the sixth week only
Ans: Thanks for reviewer’s comments. We removed the typographic errors throughout the entire text as suggested.

*pg 5 line 26 accumulating evidence indicates (not indicated)

Ans: Thanks for reviewer’s comments. The sentence (page 5; line 10) has been corrected from “accumulating evidence indicated …” to “accumulating evidence indicates …”

*rs6265 genetic polymorphism - remove genetic polymorphism throughout -could say "the BDNF variant rs6265" or "the rs6265 polymorphism"

Ans: Thanks for reviewer’s comments. We removed the typographic errors throughout the entire text as suggested.

* pg 8 line 58- should be "A linear regression model was used’ not performed

Ans: Thanks for reviewer’s comments. The sentence (page 8; line 23) has been corrected from “A linear regression model was performed …” to “A linear regression model was used …”

*pg 10 line 46- are you using variant in the place of covariates? - needs to be corrected throughout

Ans: Thanks for reviewer’s comments. The typographic error (page 10; line 16) has been corrected from “variant” to “covariates” as suggested.

*-authors should explain and clarify why they carried out a gender specific analysis

Ans: Thanks for reviewer’s comments. According to your suggestions, the following paragraph has been revised in the part of background in the revised manuscript (page 6; line 5) from: “Gender-specific effects of BNDF were further analyzed in this study” to “Previous studies found a gender-specific influence of BDNF on mood disorders [37-40]. Therefore, we wished to conduct a gender-specific subgroup analysis to find out whether the association between the BDNF variant rs6265 and emotional symptoms following mTBI is affected by gender”.
The articles are as follows:


*Authors should clarify in the discussion that the effects are short term at 1 week. Therefore there may be no long term effect of this variant-this needs to be emphasized as it is an important conclusion from the study.

Ans: Thanks for reviewer’s comments. To avoid the overstated conclusions of our findings, the following paragraph has been revised in the part of discussion in the revised manuscript (page 14; line 12) from: “This study, at least in part, provides evidence for the correlation between genetic polymorphism of rs6265 of BDNF and emotional symptoms following mTBI” to “This study, provides evidence for the correlation between genetic polymorphism of rs6265 of BDNF and emotional symptoms in the early phase after mTBI. Since our study duration range from one to sixth weeks, further studies with longer duration of follow-up are needed to elucidate the long term effects of the rs6265 polymorphism on emotional symptoms following mTBI”.

In addition, we have also revised the sentence in the part of conclusions in the revised manuscript (page 15; line 2) from: “Our study provides evidence for the correlation between the BDNF variant rs6265 genetic polymorphism and emotional symptoms following mTBI.” to “Our study provides evidence for the correlation between the BDNF variant rs6265 genetic polymorphism and emotional symptoms in the early phase after TBI”.
*-authors should comment on gender differences and speculate on the differences in the results between genders

Ans: Thanks for reviewer’s comments. According to your suggestions, we have appended the following paragraph in the part of discussion in the revised manuscript (page 13; line 12): “The gender-specific subgroup analyses revealed that the male patients carrying the T allele of rs6265 had higher scores of BAI and BDI in the both first and sixth week. The female patients carrying the T allele had significantly higher scores of BDI in the first week, whereas the difference was not shown in the sixth week. We speculate that this gender differences may be explained by the interaction between sex steroid hormones and BDNF following brain injury. Accumulating evidence indicates that estrogen regulates the BDNF expression through many several mechanisms such as methylation or directly bind to the BDNF gene via estrogen receptor [40, 44-46]”.

The articles are as follows:


