Author’s response to reviews

Title: Pilot study indicate role of preferentially transmitted Monoamine oxidase gene variants in behavioral problems of male ADHD probands.

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Answer to the comments

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Pilot study indicate role of preferentially transmitted Monoamine oxidase gene variants in behavioral problems of male ADHD probands.
Arijit Karmakar; Rishov Goswami; Tanusree Saha; Subhamita Maitra; Anirban Roychowdhury; Chinmoy Kumar Panda; Swagata Sinha; Anirban Ray; K P Mohanakumar; Usha Rajamma; Kanchan Mukhopadhyay
BMC Medical Genetics
Comments by the Editor:

1. We have noted that in additional file 3, on the second page it says "Additional file 4: Continued". Please amend this.
Answer: Necessary editing done in the file.

2. We would also like to ask for you to provide more justification for the contributions of RG, TS, SM, AR2, CKP, SS, AR3, KPM, UR, as currently they do not automatically qualify for authorship.

Ans. Contribution made by all the authors have been provided in details based on the points mentioned (line 334-341). Since all the authors were asked to review the manuscript before communication to the Journal, it would not be nice to remove any one and place under Acknowledgement section.

3. We have noted that in the Authors' Contributions section there is an AR2 and AR3, but no AR1. Please renumber these initials to AR1 and AR2, or please clarify who AR1 is.
Ans. AR2 and AR3 were given based on the affiliating institution of the authors. There is no AR1. Presently AR2 and AR3 have been mentioned using their first names (line 337 & 338).

4. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.
Ans. Done.

5. Please see the reviewers' comments below and respond accordingly to their comments.

Reviewer reports:

Pingping Zheng (Reviewer 1): The authors made necessary changes of texts in the revised manuscripts, described the sample size of each group and the manuscript was improved.
Ans. Thank you for your kind consent.

David Comings (Reviewer 2): This is a review of the revision. I find most of the revisions acceptable. I still have one issue and I confess that I am not sufficiently proficient in the finer points of statistics to know if RR completely substitutes for percent of the variance. I like percent of the variance because it is so clear. If it is one or two percent it is clear the gene in question is a minor contributor to the total picture. If the percent of the variance is greater than 5 it would be clear this was a major gene for ADHD, something p values alone cannot do. The RR values the authors report seem quite significant but the error ranges are large thus I have no real feel for the percent of the variance. If the authors could do an r2 by squaring the regression, r, between the traits and the gene variant on the more robust findings it would provide, at least for me, a more clear cut answer to the percent of the variance these genes are playing in ADHD. Mail

Ans. Thanks for the kind statement.
I would like to point out that the work presented here explored familial transmission patterns of genetic variants to the affected probands and identified those which could be considered as risk variants. Online software, UNPHASED was used for the purpose which compares the difference in transmission of the two alleles and the one showing higher transmission is considered to confer risk/associated with the disorder. In our case RR (or OR) is considered as the best option. In UNPHASED the transmitted alleles are considered as cases and non-transmitted alleles are considered as controls.

In a simple comparison between an experimental group and a control group:
• A relative risk of 1 means there is no difference in risk between the two groups.
• An RR of < 1 means the event is less likely to occur in the experimental group than in the control group.
• An RR of > 1 means the event is more likely to occur in the experimental group than in the control group.
To perform Regression analysis the two variables (i.e. X & Y) should be continuous. No categorical variable can be tested using regression analysis. For such purpose only Chi square
test (i.e. r x c contingency) is suitable. As alleles and/or genotypes are considered as categorical variable so regression analysis can’t be performed.

‘Percent of variance’ is typically used in economy and business to calculate the percent of increase or decrease (i.e. profit or loss) by comparing the present status with a previous status using simple unitary method and the outcomes (i.e. whether increased (profit) or decreased (loss)) depend on the previous status. For details you may visit http://www.dummies.com/software/microsoft-office/excel/calculating-percent-variance-in-excel/. As in our case there is no previous status (data) for the same event so as per my knowledge we can’t do this kind of test.