Reviewer’s report

Title: Association of Catechol-O-Methyltransferase Single Nucleotide Polymorphisms, Ethnicity, and Sex in a Large Cohort of Fibromyalgia Patients

Version: 2 Date: 26 May 2018

Reviewer: Wei Yang

Reviewer's report:

Remaining concerns are indicated below.

For my previous comment 3 on using statistical tests with consideration of heterogeneity effect and on suggestion to show effect size. I believe the authors have misunderstanding on statistical significance and effect size. This reference might be helpful for better understanding: Sullivan GM, Feinn R. Using effect size—or why the P value is not enough. Journal of graduate medical education. 2012 Sep;4(3):279-82.

With regard to the recommendation of using "stratified analysis" for rs6269 and rs4818, instead of simply pooling samples across heterogeneous groups, it is statistically more sound to pool the association results across groups. This is not additional "in-depth" analysis, but using statistics the right way.

For previous comment 4, the following change has been made "There were no statistically significant associations of COMT haplotypes or diplotypes with FM diagnosis in the FM group compared to the non-FM group. However, when only ethnicity was considered, there was an association of COMT diplotypes ..." Within the context of studying the association of between genetic factors and FM diagnosis, simply state there is an association could easily be misunderstood as an association with the FM diagnosis. It is worth making clear by, for example, changing to "There were no statistically significant associations of COMT haplotypes or diplotypes with FM diagnosis in the FM group compared to the non-FM group. There was an association of COMT diplotypes with ethnicity groups"

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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Yes
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Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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