Reviewer's report

Title: The genetic interacting landscape of 63 candidate genes in Major Depressive Disorder: An explorative study.

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Reviewer: Li L.S. Shen

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This paper presented an SNP-SNP interaction analysis in candidate genes for major depressive disorder (MDD). 3704 SNP-markers from the GAIN cohort including 1732 cases and 1783 controls were analyzed using three methods: two logistic regression models (multiplicative and additive) and multifactor dimensionality reduction (MDR). Although no significant interactions were identified after multiple comparison correction, several interesting top interactions were reported and discussed in the paper. The paper is clearly written and easy to follow. The methods are technically sound. The findings are informative and may have the potential to guide future studies. The following are a few comments that I hope can further improve the paper.

Minor Essential Revisions

* Figure 1: The relationship among various SNP numbers is not very clear. For example, I cannot figure out how 92 SNPs were obtained based on 34 SNPs from STAR*D, 57 genotyped SNPs from GAIN, and 28 imputed SNPs from GAIN.

* Is "SNP-SNP interactions" an independent section in parallel to the "Results" section?

* Table S2: Should "53 (4.3%)" read "53% (4.3)"?

* It seems that no significant main effect was identified. I wonder whether the top main effects (although insignificant) were in accordance with prior findings?

* Since the study did not yield any significant findings, it would be helpful to compare the top main effect findings and the top interaction findings. The major goal is to demonstrate the added value of interaction analysis in comparison to the main effect analysis.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests