1. **Notations on mathematical formulas**

We appreciate the reviewer’s suggestion in revising mathematical formulas, e.g. describing deviation and variance explicitly. We further revised the formulas that follows the mathematical norms. Specifically:

1. σ was used exclusively for deviations, whereas was used for variances.
2. δ was replaced by σ for consistent notation of deviation
3. Gaussian models were consistently described as *N(mean, variance)*, in which the second parameter is the variance
4. **P-values**

There were errors in the formula describing the P-values. The integral part accidentally showed up twice. We are thankful to the reviewer for catching this up. The revised formulas are the following:

= 2 \* , for mean() > 0

= 2 \* , for mean() < 0

We did not change the way in calculating p-values from the first to the second draft of our manuscripts.

To show in more details operating characteristics of the p-values we calculated, we took the reviewer’s suggestion in running simulation to demonstrate the p-value we computed are in general consistent with the frequentist p-values.

To do so, we built a fixed effect ordered categorical model and applied it to the top 100 variants of the ADSP study. Model parameters were estimated by both MLE and MCMC. The frequentist p-values of variant effects were calculated from the MLE estimations of expected values and standard errors, as described in the manuscript. Tail p-values were calculated from the MCMC samples by using the formulas above. We did not run this simulation on mixed models because MLE was not stable in estimating mixed models and the corresponding frequentist p-values were hard to calculate. Simulation results showed (1) the two methods report consistent expected means of variants effects (top); (2) standard error estimation of variant effect mean by MLE and standard derivation estimation of variant effect parameter by MCMC are also consistent (middle); (3) the tail p-values that we proposed are in general consistent with the standard frequentist p-values (bottom).

**Figure 1**





