Reviewer's report

Title: Antipsychotic medications and cognitive functioning in bipolar disorder: moderating effects of COMT Val108/158 Met genotype

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This is an interesting study by Arts, et al, addressing "moderating" effects of COMT Val/Met genotype on cognitive functioning in bipolar patients after antipsychotic treatment.

A candidate gene association-approach is performed.

The main finding is an association of the functional SNP rs4680 of COMT in which Val allele has a significant negative effect on composite cognitive measure after antipsychotic medications in a allelic dose-response effect.

1. Genotyping section on Page 8, the author only reported SNP rs4680 but described a panel of 184 SNPs with Sequenom Massarray in detail. I am wonder if the rs4680, the only marker identified to be associated with the trait.

2. In table 1, demographic information for ethnical group, antipsychotics used are missing. Allele freq is confusing and should be deleted and describe in the text. For Covariates listed in Table 1 is not sufficient. Antipsychotic drugs used are also the important confounding factor.

3. The author use a verb, moderate or moderating throughout the text. The better word should be modulate.

4. Power analysis is missing since case # is limited without replications.

5. Ancova test is necessary to evaluate if COMT rs4680 Val allele can predict the cognitive function outcome after treatment.

6. In Result section on page 9, quote "there were no significant differences between ... after Bonferroni correction (p<0.0042). Please explain this.

7. In introduction and discussion section, the author mentioned about the different result between SNP rs4680 genotype and bipolar comparing to Schizophrenia. What about Schizoaffective disorders? This information should be added.