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

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Reviewer: Pingping Zheng

Summary and Comments:
The manuscript investigated an Indo-Caucasoid cohort of 190 probands with Attention-Deficit/Hyperactivity Disorder (ADHD) and their parents. The ADHD subjects included 166 boys and 24 girls around eight years old. The authors genotyped a total of 58 previous reported variants from two monoamine oxidase genes MAOA and MAOB using PCR and sanger sequencing and they detected one tandem repeats VNTR polymorphism and seven SNPs of MAOA gene, and another seven SNPs from MAOB. With linkage disequilibrium analysis and association analysis of candidate alleles with ADHD trait scores, the authors stratified the population data by gender and found 3 SNPs of MAOA and 6 SNPs of MAOB significantly associated with maternal transmission to male probands and they also identified maternal transmissions haplotypes of risk alleles. They also found the young maternal age (<=26 yr) was associated with risk variants.

ADHD is much common in boys than in girls. The manuscript reported a family-based association study of Attention-Deficit/Hyperactivity Disorder (ADHD) and genetic polymorphism of two X-linked genes monoamine oxidase A (MAOA) and B (MAOB). The heterogeneity and complexity of ADHD made it difficult to identify the behavior genetic mechanisms underlying the complex disorder. The manuscript focused on analysis of two MAO genes locating in the mitochondrial outer membrane and maternal transmission in male probands. The screening and association studies might provide a few more candidate risk alleles/variants associated with this disorder. It is interesting maternal age was associated with variants from MAOA, especially rs6323 which is also a risk variant.
Minor Questions:

1. Line 55: The conclusion about preferential maternal transmissions of haplotype combinations to male were also noticed, but not observed in female probands. The female had a relative small sample size (n 24). If the authors increased the size of female cohorts, would that give a different result?

2. Sample size of subgroups was not clear in methods/results:
Line 167-176: how many subjects of each group in the following categories?
   * The male probands were divided by with or without derived allele;
   * The male probands were divided into "early onset" and "late onset" by the age <= 7 or >7 years;

3. Some sentences from the manuscript were the same or similar to the referenced papers [ref 48 and ref 49, which are the reference numbers in the manuscript]. Would the authors re-write them a little bit?

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

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics
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