Reviewer's report

Title: Genetic influences on Attention Deficit Hyperactivity Disorder symptoms from age 2 to 3

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Reviewer: Carol Van Hulle

Reviewer's report:

In “Genetic influences on Attention Deficit Hyperactivity Disorder symptoms from age 2 to 3”, the authors examine genetic contributions to stability and change in ADHD symptoms from both a quantitative and molecular genetic perspective. The paper provides some tentative support for earlier findings regarding changes in markers associated with ADHD measured at different ages in early childhood.

Individuals already steeped in the genetics of ADHD and who have a working knowledge of QTDT analysis will find this paper to be a quick and informative read. However, a general reader who is not as familiar with this literature (in particular molecular studies of ADHD) would find this paper lacking in some illuminating details. Specific suggestions and questions are listed below.

Discretionary Revisions

Title: I suggest making the title a tad more descriptive to indicate that the study includes quantitative and molecular approaches.

Abstract: Given the very weak associations between polymorphisms in 5-HTT and ADHD I don’t think it warrants mentioning in the abstract.

Wording in the top partial paragraph on page 4 is clunky. I think you mean “In addition to this analysis, we have …”

Minor Essential Revisions

Method: By parents, do the authors mean that both parents rated the twins' behavior? Please clarify. How many ratings were completed by mothers? How many completed by fathers?

Results: Indicate for which age the DAT1 marker is significant after applying a bonferonni correction.

Tables: Please indicate in Table 1 which SNPS were excluded from analysis. Also, for ease of comparison, put markers in same order in Tables 1 and 3 and use the same labels for each marker.

Major Compulsory Revisions:

Introduction:

Given that BMC does not have space constraints, I think that readers who are
not as versed in the genetics of ADHD would benefit from a more detailed description of the gene systems implicated in ADHD. What is known about the functions of genes previously implicated in ADHD symptoms for example? Are recent GWAS studies based on children or adults? What selection criteria did you use to pick potential markers?

Method:
I count 10 SNPS from Table 1 missing from Table 3. Why does the text state that 9 were dropped from analysis? Is it normal to have 1/3 of your SNPS fail? What does this say about the quality of your data?

Was gender a covariate in the QTDT tests?

A more complete discussion of the relationship between AT, AW, AP and implications of significance among these tests might help the reader navigate the results and discussion section.

Results: In the methods it states that a cholesky decomposition was fit to the data, but then a correlated factors model is presented on page 7 in the results (and in the figure)? Why report a correlated factors model when the cholesky provides essentially the same information but more directly addresses the authors questions about change and stability in ADHD? Also, please include the bivariate heritability (and analogous environment parameters) in Table 2.

Why was the AW test not performed for NET1 rs11568324?

**Level of interest:** An article whose findings are important to those with closely related research interests

**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.