Reviewer’s report

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

Version: 1 Date: 30 April 2010

Reviewer: Ian Gizer

Reviewer’s report:

In their manuscript entitled “Genetic influences on Attention Deficit Hyperactivity Disorder symptoms from age 2 to 3,” the authors present data from a twin sample suggesting that common genetic influences underlie most of the variation in ADHD symptoms at these two time points, but demonstrate that age-specific genetic influences are involved as well. They provide additional support for this conclusion by conducting tests of association between ADHD symptoms and specific polymorphisms in a set of candidate genes.

This is a very interesting and well-designed study that draws its greatest strengths from the use of a longitudinal twin design to conduct both quantitative genetic analyses examining the genetic etiology of ADHD as well as tests of association with specific polymorphisms. The report is well-written, the analyses are appropriate for the questions asked, and the conclusions accurately reflect the results of the analyses. Nonetheless, there are some points that require clarification, which are outlined below.

Major Compulsory Revisions:

1.) Some basic information regarding the study sample does not appear to be included. Specifically, what was the gender composition of the sample and what were the basic distributional properties (mean, standard deviation) of the CBCL hyperactivity and Rutter scales?

2.) For the twin analyses, the authors provide statistics regarding relative fit when contrasting specific models, but statistics regarding absolute model fit are not provided. Such statistics are typically provided, and the authors should either include them or present a justification for not doing so.

3.) As part of the twin analyses, the authors present data from the Cholesky decomposition model suggesting that the ‘C’ parameter was estimated at zero. Did the authors formally test this by trying to drop this parameter from the model?

4.) The authors should provide an explanation of how the QTDT software program handles the presence of MZ twins in the analysis. I’m not sure that the general reader will be familiar enough with the program, and thus would benefit from an expanded description.

5.) The authors describe applying a Bonferroni correction to the AW results to
correct for multiple testing, but no such correction is discussed for the AT results. Given the number of polymorphisms that were tested, this should be included.

Minor Essential Revisions:

1.) For the association analyses, the degrees of freedom reported for each test appear to reflect sample sizes rather than the degrees of freedom.

2.) On page 7, the authors report a p-value = 0.00. This should be reported as <.01.

**Level of interest:** An article of outstanding merit and interest 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