Reviewer's report

Title: Dopamine transporter 3'UTR VNTR genotype is a marker of performance on executive function tasks in children with ADHD

Version: 1 Date: 27 October 2007

Reviewer: Rosemary Tannock

Reviewer's report:

General

The study addresses an important area of investigation: namely genetic contributions to cognitive functioning in ADHD. To do so, the investigators have recruited a large sample of children with ADHD, whose diagnosis was confirmed using a systematic and comprehensive diagnostic protocol. Also, the investigators administered three established neuropsychological measures of executive functioning. Thus on the one hand the methodology is strong, but on the other hand the specific neuropsychological tests selected implicate a wide range of executive and non-executive functioning. Moreover, the use of more general or averages dependent measures (e.g., WCST total errors rather than conventional perseverative errors; overall FFDI rather than separate scaled scores of Digit Span and Mental Arithmetic) may obscure more specific links between genotype and type of executive function. Furthermore, although the positive findings are encouraging, they are puzzling. As noted by the investigators, current findings regarding effects of DAT genotype on cognitive function are inconsistent. One concern here is that this study does little to clarify the confusion. Many studies have found poorer cognitive performance in carriers of the 10/10 genotype. By contrast this study found poorer cognitive performance in carriers of the 9/10 genotype not only in the opposite direction to findings from previous studies, but also are difficult to interpret. Clarification of various issues listed below may allow this study to contribute novel and important information about genetic factors implicated in the cognitive problems associated with ADHD. Despite, my criticisms, this work is important and the investigators are congratulated on attempting to answer important but difficult questions.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. On page 12, authors report frequency of 10- and 9-repeat alleles were 71% and 29% respectively, (abstract reports 196 children), but data reported in Table 1 would suggest that 52% of sample carry the 10/10 genotype and 39% carry 9/10 genotype. Need s clarification.

2. On p.13 authors state that children with 10/10 genotypes had scores within the normal range of FFDI as well as WCST. However, summary data presented in Figures suggest that children in 9/10 genotype group also had scores in normal
range. Was there any difference in proportion of children in each genotype groups who had scores on FFDI and WCST in clinical range? Moreover, if FFDI data represent scaled scores, then appears that most in average to above average/superior range, so cannot talk about impairment. This requires clarification.

3. Present scatter plots with mean to provide more detailed view to ascertain whether findings attributable to a few outliers;

4. WCST scores – Present data for total #categories completed and #trials to first category, since errors tend to be inevitable if take longer to identify first category (color). Were there group differences in total number of categories completed or # trials to completing first category? Were these data linked to genotype?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

1. Table 1 reports mean number of DSM-IV ADHD symptoms as assessed by DISC-IV. Would be more helpful to present mean number of inattentive and hyperactive/impulsive symptoms separately.

2. It would be more helpful to readers to present DS and Arithmetic separately;

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance 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.