Reviewer's report

Title: No Evidence for the Association of DRD4 with ADHD in a Taiwanese Population
Within-Family Study

Version: 1 Date: 7 February 2005

Reviewer: Stanley F Nelson

Reviewer's report:

General

The authors test if polymorphisms in or near DRD4, described in the literature and tested on many different datasets, are associated with ADHD in trios from a Taiwanese population using TDT analysis. 212 trios are tested which should provide sufficient power to provide a meaningful contribution. TDT is an appropriate method to employ, and generally the paper is clearly presented and the data sound. Some additional clarification of the methods and samples are needed, as well as additional discussion to place the work in perspective. The overall discussion of the paper and referencing, with the exceptions noted below are really quite good and thorough. The writing is clear. The results section is short but appropriately so.

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

1) The authors include individuals affected with ADHD with IQs under 70. I would recommend removing this 13% of their dataset and repeating the TDT analyses. Given the lack of biased allele transmission, this small reduction in the sample size is unlikely to alter the conclusions of the paper.

2) Further the authors indicate that 78% of the sample is combined subtype while 22% had the inattentive subtype. Can the authors describe if this distribution of affection status is common across the different populations studied at DRD4 polymorphisms? That is are the previous association results driven by "pure" inattentive subtype individuals which are relatively rare in this current study?

3) Since the authors use standard methodologies, the work is cursorily described. The authors should indicate what methods were applied to the data to remove genotyping errors and the number of samples removed. The 48 bp repeat can be difficult to accurately call. Are the genotype in HWE? Are there mendelian errors detected? What is the rate of detection?

4) Finally, while the work shows that there is no biased transmission of alleles in the 48 base repeat nor in the promoter region in/del polymorphism, the work does not indicate that DRD4 is not a risk allele in the Taiwanese. This is a bit of a description issue. The authors should lessen the claim to just these polymorphisms in the Taiwanese population.

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

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Discretionary Revisions (which the author can choose to ignore)

While the results are “negative,” it is important to publish substantial datasets in various populations to obtain a more complete picture of risk alleles in ADHD. However, the same definition of ADHD (DSM-IV) applied throughout the world is likely to result in somewhat different affected populations due to societal norms. Do the authors think that ADHD may simply be scored differently in Taiwan than the other populations studied? This would be useful to place in the discussion section.

What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests