Reviewer’s report

Title: The 5-HTTLPR polymorphism of the serotonin transporter gene and short term behavioral response to methylphenidate in children with ADHD

Version: 2 Date: 19 February 2009

Reviewer: Tobias J. Renner

Reviewer’s report:

1. Is the question posed by the authors well defined? yes
2. Are the methods appropriate and well described? the authors are advised to do some improvement here, please see the comments on this
3. Are the data sound? the figures given are no good visualisation of the reported statistical findings.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? yes
5. Are the discussion and conclusions well balanced and adequately supported by the data? conclusions should be stated more carefully
6. Are limitations of the work clearly stated? yes
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? it seems
8. Do the title and abstract accurately convey what has been found? according to the reported statistical findings yes
9. Is the writing acceptable? language: well written

However, some points have to be stated:
In general literature cited is quite "antique", more recent work has to be included and discussed! e.g.: gene effect sizes: Faraone and Khan 2006, 5HTT and symptom dimensions: Mick et al. 2009, Oades et al. 2008, Biederman et al. 2008.

Findings of Tharoor et al. 2008, Zeni et al. 2007 on the investigated subject have to be cited and included!

Major point: In the introduction there is a substantial error: 5HTT is located on 17q11 not 17p11!!

The introduction is quite lengthy.

Methods:

was there a wash out period for the cross-over groups after 2 weeks?

Genotyping: for a future evaluation of the functional triallelic variation there should be mentioned, how the distribution of la- and lg-alleles was

Results:

the “effects” of clinical intervention could also be based on the expectancy of the raters (parents and teachers) knowing about that intervention instead of objectively improved behaviours.

Major point: suddenly an statistical analysis on the DAT VNTR appears without prewarning in the introduction or methods! To avoid the impression that analyses have been made rather randomly than guided by hypothesis the reason why this is included here should be explained properly and in the proper sections, earlier than the discussion.

Discussion:

Major point: negative findings by Tharoor et al. 2008, Zeni et al. 2007 have to be discussed!

CGI-T does not underline the reported effects. There seems to be only a marginal difference in between the genotype groups and response to MPH.

Reference list:

6): Year is incompletely cited

In general the manuscript provides interesting data and should be considered for print after having revised the mentioned issues and after having been updated to the contemporary knowledge.

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