Reviewer’s report

Title: Monoamine related functional gene variants and relationships to monoamine metabolite concentrations in CSF of healthy volunteers

Version: 3 Date: 17 February 2004

Reviewer: Redford Williams

Reviewer’s report:

General
The authors have responded very well to my suggestions. In their letter responding to my review they indicated that evaluation of the interaction between the DBH and MAOA polymorphisms did reveal some evidence of an interaction affecting 5HIAA and HVA concentrations among women, but also expressing their preference not to include these results in the present report, because of very small cell sizes. This is reasonable, but I note the possible interaction here, because there may be others in a position to evaluate it with larger cell sizes. The findings of significant molecular heterosis for the DBH-1021C/T variant’s association with 5HIAA and HVA concentrations are both interesting and daunting, for they force us to acknowledge, as the authors do in the revised ms, just how complex these gene effects can be.

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

None

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

None

Discretionary Revisions (which the author can choose to ignore)

In view of the heterosis effects of the DBH-1021C/T variant, it is probably not appropriate to pool the T/T and C/T genotypes and then conclude that higher 5HIAA and HVA levels are associated with "the -1021T containing genotypes." The heterosis indicates that it is the heterozyote containing BOTH the C and the T allele that is associated with higher 5HIAA and HVA concentrations, not the presence of the T allele.

What next?: Accept after discretionary revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests: None