Author's response to reviews

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

Authors:

Dr Erik G Jonsson (erikj@ks.se)
Jessica Bah (jessica.bah@pharm.gu.se)
Jonas Melke (jonas.melke@pharm.gu.se)
Rami Abou Jamra (rami.aboujamra@uni-bonn.de)
Dr Johannes Schumacher (johannes.schumacher@uni-bonn.de)
Lars Westberg (lars.westberg@pharm.gu.se)
Roland Ivo (Roland.Ivo@gmx.de)
Sven Cichon (Sven.Cichon@uia.ua.ac.be)
Peter Propping (propping@uni-bonn.de)
Markus M Nothen (mnoethen@uia.ua.ac.be)
Elias Eriksson (elias.eriksson@pharm.gu.se)
Goran C Sedvall (goran.sedvall@ks.se)

Version: 4 Date: 4 Mar 2004

PDF covering letter
Comments to remarks by referees regarding

MS 9328548262263015: Jönsson et al, "Monoamine related functional gene variants and relationships to monoamine metabolite concentrations in CSF of healthy volunteers"

REFEREE 1

We thank the reviewer for taking his time to re-review our manuscript and finding that ‘the authors have responded very well’ to his suggestions. Regarding the additional point raised by the reviewer:

DISCRETIONARY REVISIONS (which author can choose to ignore)

The referee points out that in view of the heterosis effect 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 levels of 5-HIAA and HVA are associated with the –1021 T genotypes.

We would argue that this has not been concluded, see the Conclusions section and Conclusions in the abstract. However, we have discussed (in the Discussion section) different possibilities including those mentioned by the author. In the same paragraph we also discuss the possibility of a more complex physiological pattern, as suggested by the higher p-values obtained when the analyses was performed pooling homozygotic genotypes. Given the associations that were found in the analyses pooling T/T and C/T genotypes, we do not find it inappropriate to discuss also these possibilities. In order to further emphasise the stronger results obtained pooling heterozygotes we suggest the following minor changes in the fifth paragraph of the Discussion section (see below). With this we feel that this topic is reasonably balanced.

Changes in the discussion section (underlined has been added, within paranthesis deleted): “… This is in accordance with the theory that a less effective conversion of dopamine to norepinephrine would lead to higher amounts of dopamine, and in turn to its degradation product HVA. However, the stronger associations between heterozygotic genotypes and 5-HIAA and HVA concentrations, examples of positive heterosis [52], (may) rather indicate a more complex physiology including interactions based on hidden stratification of unknown factors or heterozygotic advantage [52].”