Reviewer's report

Title: Glutathione S-Transferase omega 1 variation does not influence age at onset of Huntington's disease

Version: 1  Date: 2 February 2004

Reviewer: Luc Djousse

Reviewer's report:

General
This is a null finding paper. Nevertheless, findings could be summarized as a brief report.

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

1. Statistical analyses: The authors present crude analyses relating glutathione S-transferase polymorphisms to age at onset (AO) of HD. It is established that AO is influenced by the size of CAG repeat and we have recently demonstrated that normal and expanded CAG repeats interact to influence AO (Djousse et al.2003). Thus, it is important in any association study of AO to account for repeat size. One way of achieving this is to use analysis of covariance to estimate adjusted means of age at onset (adjusted for CAG repeat size and perhaps normal repeat and their interaction) and evaluate whether these means differ by GSTO genotypes. the statistical methods utilized in the manuscript should be clearly indicated in text.

2. The best fit of the association between AO and repeat size if log-linear (myers et al.). I would recommend the use of log-transformed AO in the regression model instead of crude AO and present geometric means.

3. The number of HD patients described in the methods (n=232) is different from that reported on the figure 1 a/b (n=143) and no explanation is provided. The authors should explain what happens to the other 89 HD subjects not included in the graph.

4. The conclusion is missing. After the discussion, a brief conclusion should reiterate the lack of an association between GSTO and AO.

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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)

1. Figure 1: label used on the x-axis is not defined in text (101, 102, 202). It is unclear what these numbers are referring to.

2. In the study design, the authors used 228 controls. What is the role of controls since they did not play a role in the main analysis? Evaluation of AO of HD according to GSTO genotypes presumes that subjects have been diagnosed with HD.

3. Table 1: the way genotypes for GSTO1 and GSTO2 are presented is a bit confusing. One might think that haplotypes are presented.

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Discretionary Revisions (which the author can choose to ignore)

1. Abstract: the section on "background" can be shortened to 2-3 sentences and the conclusion should be specific to the 2 SNPs examined.

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: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:
None