Reviewer's report

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

Version: 1 Date: 12 February 2004

Reviewer: Alexis Brice

Reviewer's report:

General
The authors have studied the distribution of a single nucleotide polymorphism in each of the glutathione S-Transferase W 1 (GSTO1) and 2 (GSTO2) genes, as well as their potential effect on the age at onset in Huntington's disease. Although it is clear that the size of the repeat expansion in the gene responsible for Huntington's disease (HD) does not account for all of the variability in age at onset, the authors do not provide strong evidence explaining why the GSTO1 and 2 genes would account for age at onset in HD. In a series of 232 patients and 228 controls, there were no significant differences in the allele and genotype frequencies. The contrary would have been surprising given that the disease is caused by a gene defect located in a chromosomal region that is not linked to the genes tested. In addition, in a subset of 143 patients for whom the age at onset of motor signs was known, there was no evidence for an effect of the genotypes at these two SNPs on this variable. These results indicate that the two SNPs tested do not account for a detectable effect on the age at onset variability in HD.

Major Compulsory Revisions

1- Concerning the first part of the study, which is not really justified given that the cause of the disease is known, the authors do not indicate whether controls were matched with patients in terms of sex, age and geographical origin.
2- The authors over interpret their results when they state that the "chromosomal region of GSTO1 and GSTO2 flanked by the investigated SNPs is not a candidate region for a major susceptibility allele influencing the age at onset in HD". In fact, the authors have only excluded the responsibility of the two SNPs tested (for a given statistical power). They cannot exclude the possible influence of other polymorphisms in these genes, which would not be in linkage disequilibrium with those tested.

Minor Essential Revisions

Accept after minor essential revisions

What next?: Accept after minor essential revisions

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No