Reviewer's report

Title: Failure to confirm influence of Methyltetrahydrofolate reductase (MTHFR) polymorphisms on age at onset of Huntington disease

Version: 1 Date: 14 June 2005
Reviewer number: 2
Reviewer's report:

General

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. Studied population needs to be clarified. Authors indicated that 167 patients were used for analyses. However, in the method section, the investigators indicated that "all patients and controls gave informed consent". Who were these controls? Were they part of the 167? How were they selected?
2. Given the fact that several siblings could be diagnosed with HD, it is important to know if subjects in this study were independent (one individual per family). If not, the authors need to use appropriate statistical method to account for familial clustering.
3. Was the distribution of the studied SNPs in HWE?
4. Please provide means for age at onset according to genotypes of studied SNPs. This is important in that the direction of effect can be observed in a non-statistically significant result. Since the log-transformed age at onset (AO) is a better fit than untransformed AO, the authors might consider using Ln (AO).
5. Discussion should include a paragraph about small sample size as a limitation and perhaps lack of power to detect difference as possible explanation of these findings.

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. Include sample size in abstract.
2. Revised the title to account for small sample size (lack of appropriate power to detect an effect). "Failure to confirm .." assumes that the study had enough power to detect a difference.

Discretionary Revisions (which the author can choose to ignore)

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, the manuscript does not need to be seen by a statistician.