Reviewer’s report

**Title:** Association of HFE common mutations with Parkinson’s disease, Alzheimer’s disease and Mild Cognitive Impairment in a Portuguese cohort

**Version:** 1 **Date:** 21 March 2006

**Reviewer:** Cornelia Van Duijn

**Reviewer’s report:**

**General**

The authors studied the association between two common polymorphisms in the HFE gene and Alzheimer’s disease, Parkinson’s disease and Mild cognitive impairment. They found that homozygosity for the C282Y and H63D mutations are not associated with AD, PD and MCI. However they report that heterozygosity for the C282Y mutation is associated with an increased risk of PD.

This paper attempted to clarify a conflicting literatures on the association between iron, HFE mutations and neurodegeneration. However their study sample, study design and report do not achieve the objective of final clarification of conflicting literature evidence.

-----------------------------------------------------------------------------------------------------------------------------------

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

In the introduction, there is no literature review or reference to why the looked at MCI.
In the results section, the authors report testing the CORRELATION. They probably meant association or relationship. Statistical correlation is a different kind of test.
What is the interpretation of the difference in allele frequency between AD and PD patients that the authors report?

The explanation given to the difference in results between various study by the authors is linkage disequilibrium in the same gene or linkage disequilibrium in diverse populations. Their explanations do not follow and it is hard to accept this since all studied mentioned studied the same gene variants.

-----------------------------------------------------------------------------------------------------------------------------------

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

In the Introduction, the authors refer to HFE as a disease and a gene at the same time... “HFE is most often caused by mutations in the gene HFE....” AISO, ….compound heterozygosity for these mutations appear to be at risk for HFE... They mean hemochromatosis?
In the discussion, the authors refer to the paper of Dekker et al as reporting no association between HFE and PD but points to reference No 20 which is another paper. The sentence following refers to Dekker et al paper. Please check and correct.

There is a need for an improvement in the English used throughout the manuscript.
Discretionary Revisions (which the author can choose to ignore)

The sample size is not large and powerful enough to reach definitive conclusions. The selection of patients is not clearly explained. What do the author mean by AD patients were SELECTED from a larger sample SELECTED in a consecutive manner. What was selected and from what is not clear from this sentence. What were the selection criteria and from what sample, what source? Is it possible that relative living in the same are and coming to the same clinic were included? The author did not specify how the control group was recruited.

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 limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests