Reviewer's report

Title: The dopamine beta-hydroxylase -1021C/T polymorphism is associated with the risk of Alzheimer's disease in the Epistasis Project

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Reviewer: Benedetta Nacmias

Reviewer's report:

In this study, Combarros and colleagues have evaluated the impact of the -1021C/T polymorphism (rs16111115) of dopamine β-hydroxylase (DBH) on Alzheimer's disease risk in over 8000 subjects of the Epistasis Project. They also evaluate the correlation of DBH SNP and polymorphisms of the pro-inflammatory cytokine genes, IL1A and IL6. They found that the presence of the -1021T allele was associated with AD, sex and age related. In fact it resulted nearly restricted to men < 75 years old. Moreover they found an interaction between the presence of DBH -1021T and the -889TT genotype (rs1800587) of IL1A.

This manuscript makes an important contribution to understanding genetic susceptibility of AD.

The question posed by the authors is well defined. The sample size of the investigated population (1,757 AD patients and 6,295 elderly controls) is adequate and the results together with the quoted literature contribute to define this polymorphism as associated with AD.

It is a straightforward neat paper grounded on a reliable clinical and laboratory methodology.

Some minor essential revisions are here below reported:

1) In Additional table 1: 6294 total subjects are reported in the table, in the text they are 6295. please control.

2) Additional table 2: the title must be changed: … genotypes distributions …instead of genotype frequencies

Moreover as for the different studied SNPs the number of samples is not always the same it should be added a column with the total samples analyzed for each SNP.

3) Table 5 There appears to be a mistake for IL-174GG: Vs TC+CC should be reported also for IL-174GG (it is reported vs. GC+CC)

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.