Reviewer's report

Title: Role of the H1 haplotype of microtubule-associated protein tau (MAPT) gene in Greek patients with Parkinson's disease

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Reviewer: Rohan - de Silva

Reviewer's report:

The authors report on their study of the association with Parkinson's disease (PD) of the tau gene (MAPT) H1 haplotype. This confirms in a Greek case-control group the findings from several previous studies, meta-analyses and a recent genome-wide association study (Pankratz et al 2009, Hum Genet). Although there are some exceptions, it appears from this, and the majority of studies that the main effect of the association of H1 with PD is explained by the H1/H2 division alone and, unlike in PSP and CBD, not due to underlying sub-haplotypes of H1. In addition to the H1/H2 clades, the authors genotyped two SNPs, haplotypes of which were shown to be associated with PD in two previous studies. Not surprisingly, they failed to show associations with these SNPs and their haplotypes.

The choice of only two "H1-SNPs" in addition the the H1/H2 division would not account for the entire diversity of the MAPT locus in their study population and coverage is therefore incomplete. A more comprehensive approach would be to identify/genotype haplotype-tagging SNPs representative of the Greek population. The authors should discuss this and also describe the SNPs in context with previous studies and their location within MAPT (eg rs242562 is in LD with rs242557). Noting that the PD cases are all clinical, the authors should discuss the possibility inclusion of misdiagnosed PSP cases. The authors could cite our recent paper (Vandrovcova et al, Neurobiol Aging doi:10.1016/j.neurobiolaging.2007.11.019) where we carried out a study with pathologically confirmed PD cases, using a tagging SNP approach, and we also showed that the association is chiefly driven by the H1/H2 division alone.

Page 6, line 12: H1H1 > H1H2
Use the rs numbers for SNPs 1 and 2 throughout the text and tables.

Level of interest: An article whose findings are important to those with closely related research interests

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.