Reviewer’s report

Title: Lack of association between Cathepsin D C224T polymorphism and risk of Alzheimer’s disease: An update meta-analysis

Version: 3
Date: 29 October 2013
Reviewer: Timothy Hohman

Reviewer’s report:

Major Compulsory Revisions:
The biggest concern as a reviewer is still in understanding why the stratified results (specifically the Caucasian results) differ from the Schurr study. The authors could bolster this discussion by highlighting exactly which datasets differ between the two studies. It appears the 4 Asian population datasets (as the authors highlight) along with the Albayrak, 2010 study which was not included in Schurr and the Mateo 2002 study which was excluded from the Schurr analysis for HWE. Is the difference between the Schurr result in caucasians and the present result in caucasians simply due to the addition of these two datasets? Given this study and the Schurr study are largely the same in terms of the caucasian samples, it seems essential for the author’s to explain why their result differs from that of Schurr in specific rather than general terms.

As mentioned previously, the author’s highlight the trend in APOE carriers (Table 3, p = 0.072) in their discussion, yet fail to report a similar trend in Caucasians when using a dominant model (Table 2, p = 0.082). It would seem more fair in the discussion on page 13 to state: "a trend was present in Caucasians when using a dominant coding (p = 0.082)" similar to the way in which the APOE results are summarized. Even better, the authors could choose not to report either nominal trend in the discussion.

Additionally, the author’s should report the p-value when they remove the 2 studies that violate HWE, paritcularly given this was the explanation given by Schurr as to why their results differed from previous meta-analyses.

Minor Essential Revisions:
Table 2 appears to have some inconsistencies. It reports 23 studies in the overall analysis (Table 2 row 1 and 2), yet 25 studies are present when stratifying (21 caucasian and 4 asian). The forest plot also shows 25 studies, so presumably this is just a typo in table 2.

It also is not clear why all studies do not fall into either LOAD or EOAD. Was this due to a lack of age of onset data for the other 13 datasets?

Fix abbreviations throughout (i.e. EOAD and LOAD rather than EAOD and LAOD)
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