Reviewer's report

Title: Plasma 24S-hydroxycholesterol is increased in late onset Alzheimer's disease but not in vascular dementia

Version: 2 Date: 2 July 2011

Reviewer: Benjamin Wolozin

Reviewer's report:

This manuscript investigates the relationship between plasma 24S-OH-Chol and dementia. The authors note that levels follow a rank order of: LOAD>CIND>VA dementia>Ctrl. They also examined 24S-OH-Chol/TC and observed statistically significant differences. Finally, they examined numerous psychological tests and observed modest correlations between 24S-OH-Chol/TC and some of the psychological tests. This study is interesting but the correlations that rely on the ratio of 24S-OH-Chol/TC are dubious because these two pools of molecules are regulated independently. TC levels reflect dietary intake and peripheral TC synthesis, while 24S-OH-Chol levels largely reflect brain cholesterol catabolism (with some input from heart and muscle). Thus, although the data are interesting, the rationale for investigating such a ratio is dubious.

Major compulsory revisions:

The discussion must be modified to clearly state the weak rationale for evaluating samples based on such a ratio. The current discussion fails to address any of the ambiguity.

Minor essential revisions:

Page: 9
The results should note that the prevalence of females was highest in the LOAD group.

Page: 12
The relationship between 24S-OH-Chol/TC and inflammation cited in the discussion needs to be corrected for the levels of 24S-OH-Chol. Typically, in vitro studies use levels of 24S-OH-Chol that are much higher than the levels existing in vivo.

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests.