Reviewer's report

Title: Immunohistochemical study of N-epsilon-carboxymethyl lysine (CML) in human brain: relation to vascular dementia

Version: 2 Date: 16 July 2007

Reviewer: Geert Jan J Biessels

Reviewer's report:

General

The authors have made a number of relatively minor modifications to the paper. There are, in my opinion, still important problems related to this paper. The principal aims are now defined more clearly in the abstract and the introduction (Nevertheless, on page 15 of the discussion the authors still appear to redefine their “major goal” by leaving out the RAGE ligand expression in neurons). Questions still remain with regard to the definition of the study population and the principal outcome measures.

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

1. The study population needs to be defined more clearly. Apparently the authors included 25 patients from a series of approximately 240 autopsies. Did the authors randomly select 25 patients that met criteria 1 to 3 as defined on page 7? Are these the first 25 patients that met the criteria; if so, how many individuals were screened with these criteria? Did all other 215 patients not meet criterion 1 to 3? What was the dementia type in the included individuals?

2. The outcome measures need to be defined more clearly.

I repeat from my previous comment: The introduction addresses AGEs in relation to microvascular damage. In the methods section the authors describe the sampling of 10 “vessels” in the white matter and the basal ganglia. What kind of vessels? Capillaries, large arteries? Arterioles?

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

1. The results section still contains some rather redundant analyses: if CML staining is related to dementia and the classification of dementia is based on the CAMCOG the relation of CAMCOG scores with CML staining is not surprising.

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Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**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:**

no conflicts of interest