Author's response to reviews

Title: Population studies of sporadic cerebral amyloid angiopathy and dementia: a systematic review

Authors:

Hannah AD Keage (hk323@medschl.cam.ac.uk)
Roxana O Carare (R.O.Carare@soton.ac.uk)
Robert P Friedland (robert.friedland@case.edu)
Paul G Ince (P.G.Ince@sheffield.ac.uk)
Seth Love (seth.love@bristol.ac.uk)
James A Nicoll (J.Nicoll@soton.ac.uk)
Stephen Wharton (s.wharton@sheffield.ac.uk)
Roy Weller (row@soton.ac.uk)
Carol Brayne (cb105@medschl.cam.ac.uk)

Version: 2 Date: 14 November 2008

Author's response to reviews: see over
To the editor, BMC Neurology,

Please see attached revisions to the paper ‘Population studies of sporadic cerebral amyloid angiopathy and dementia: a systematic review’ (MS: 8547908872180037). Changes to the manuscript are indicated in italics.

Yours sincerely,
Dr Hannah Keage

REVIEWER 1

Major compulsory revisions

Comment 1: P5 second paragraph (Background)
Definition of CAA: CAA is the deposition of Abeta …in the media and adventitia of small and medium-sized cerebral cortical and leptomeningeal arteries and capillaries. In addition, it is accepted that veins may also be affected (Vinters H 1987: Stroke 18; 311-9).
Response: This has been incorporated and the sentence now reads: “CAA is the deposition of the amyloid peptides, of which Aβ is the most common, in the media and adventitia of small to medium-sized cerebral and leptomeningeal arteries, and less commonly in the walls of capillaries and veins [2-5].”

Comment 2: P7 (Methods)
The authors report that six studies were identified as being fully population based. However, only five are reported here; the HAAS -study (Pfeifer et al) is missing in the list.
Response: The authors thank the reviewer for pointing this out. The HAAS study has now been included and the sentence reads: “the Hisayama study (Japan), Vantaa 85+ (Finland), the Cambridge City over 75 Cohort (CC75C; England), the Honolulu-Asia Aging Study (HAAS; USA), the Cache Country study (USA) and the MRC Cognitive Function and Ageing Study (CFAS; England and Wales).”

Comment 3: P15 & P16 (Discussion)
The style of references: (Chalmers et al., 2003; Eng et al.,2004, Greenberg et al., 1995; Nicoll et al., 1996) and (Greenberg, Bacskai, and Hyman 2003, and Eng et al., 2004, and Greenberg et al., 2003), does not correspond the reference style.
Response: These references have been changed.
Discretionary revisions

Comment 4: P12 (Discussion)
The authors discuss factors leading to varying incidence rates for CAA: the methods used in diagnosing dementia; the age of the individuals in the studies, and the staining methods used to diagnose CAA. Three additional factors may be added: I) Studying both cortical and leptomeningeal CAA versus cortical CAA only. This is relevant in determining the total CAA score, as mild CAA may be present in leptomeninges only. However, severe CAA almost always is also cortical. II) Scoring (grading) of CAA, i.e. grades 0-3 versus grades 0-4, and how the limits for each grade have been set. III) The cerebral regions studied (being discussed also later).

Response: These points have been integrated into the discussion (P14 para 1) and reads: “The selection of parenchymal and/or leptomeningeal samples is also important, as CAA severity is usually higher in the later [54]. The choice of cortical region(s) and the grading system employed in the scoring of CAA in terms of its scale (i.e., 0-3 or 0-4) and definition of severity, would have also contributed to inter-study variability.”

REVIEWER 2

Minor Essential Revisions

Comment 1: P5 para 2-P7 line 2
Although there is a strong association of AD with CAA, previous reports suggesting CAA to be an independent risk factor for dementia were not supported except for a subgroup lacking any AD-related pathology.

Response: The authors thank the reviewer for this comment. This finding has now been stated in the introduction (P7, para 1): “CAA has been reported to affect cognition/dementia status independently of other neuropathological markers of dementia [3, 7, 12, 35, 36]. However, in one study CAA was found to be associated with dementia only in those who lacked any AD-type pathology [37].”

Comment 2: Reference 8: typos – correct: …eine Form…; …Zeitschrift…
Response: This has been changed. The reference is now:

Comment 3: Reference 39 incomplete – Acta Neurol Scand 114
Response: This has been changed.

Comment 4: Reference 100 not found
Response: Reference 100, now 103, can be found at http://www.ncbi.nlm.nih.gov/pubmed/16281911.

Comment 5: P15 line 3; P16 para 2
References should be replaced by numbers.
Response: This has been changed.