Reviewer's report

Title: Chronic cerebrospinal venous insufficiency in Multiple Sclerosis: an highly prevalent age-dependent phenomenon without clinical correlations

Version: 2 Date: 22 September 2012

Reviewer: Paolo Zamboni

Reviewer's report:

This is an excellent paper and the Authors should be congratulated. However, the conclusion proposed by the Authors cannot be drawn on the basis of either cross-sectional design or updating literature; consequently, the discussion section have to be better addressed and modified accordingly.

MAJOR COMPULSORY REVISION

1. The actual results interpretation of the Authors is “CCSVI in MS is the consequence of earlier vein wall ageing due to MS inflammation”. Unfortunately, such conclusion is ultimately challenged by the only published histology paper. Coen et al. did not find more inflammatory markers in the MS jugulars respect to controls. Thus, the authors have to delete the last abstract sentence, and substitute with … to elucidate our results further research and longitudinal data are needed, or something like this.

2. In chronic venous disorders of legs (update reference list) haemodynamics and disease severity become more pronounced with ageing, exactly as in CCSVI. Do the Authors think qualitative Doppler Zamboni criteria adequate to detect small quantitative changes at the beginning of the story? Do the Authors believe that a more precise and sophisticated assessment is necessary to solve if CCSVI is cause or product of MS? Do the Authors warrant longitudinal studies?

3. Authors conclusions are further challenged by CCSVI detection in paediatric MS and CIS ref#10, as well at onset with a prevalence 8times higher ref#12 plus letter of Avruscio on Annals not cited, yet.

4. The discussion section should be re written admitting that the study cannot permit to draw conclusions on the Authors’ original findings. The Authors should discuss both their first conclusion and what is above reported at hypothesis level. Literature needs to be up-dated.

MINOR ESSENTIAL REVISION

1. Title. Limit the title to the two main findings, higher and ageing dependent prevalence of CCSVI in MS.

2. Introduction line 4. Perfusion problem is a fact that cannot be explained with the immune response in MS (D’Haessler Lancet N 2011). In addition, perfusion is a central point in CCSVI because worse perfusion was found in CCSVI HC (Radiology 2012) as well as related to CCSVI in MS (BMC Medicine 2011). Please update.
3. Do the Authors think perfusion problems possibly related to neurodegeneration?

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Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

My University received technical equipment by Esaote Biomedica