Reviewer’s report

Title: Chronic cerebrospinal venous insufficiency in Multiple Sclerosis: an highly prevalent age-dependent phenomenon

Version: 3 Date: 20 November 2012

Reviewer: Marian Simka

Reviewer’s report:

Major Compulsory Revisions:
1. Abstract. Background. It should begin with: „The aim of our research was to investigate…..”
2. Abstract. Such term like “as previously described” should not be found in an abstract. The sentence should be rewritten.
3. Abstract. The authors should unequivocally state which correlation (positive or negative) has been found between the patients’ age and presence of CCSVI.
4. Abstract. “flux” is the Italian word. The proper English term is “flow”.
5. Abstract. The authors should not use the term “criterion 4” outside the context. Such a term may be used in the main text. On the contrary, an abstract should be an autonomous document, easily understandable with access to the main text.
6. Abstract. It would suggest to delete the last sentence. It bears no information. Instead, the authors may give more information (within word limit) in the Results section.
7. Abstract. Abstract should be proofread (English is poor).
8. Background. The authors are citing small venographic studies (ref. 4, 5, 6), but big ones are not cited. Such studies should also be included.
9. Results. Clinical characteristics of the patients should be presented first (“MS patients belonged….), then the results of sonography (“A concordance between…..”)
10. Results. “flow” instead of “flux”
11. Results. The authors should explain how the CCCSVI presence was related to age (positively or negatively); correlation coefficients, in addition to p values, will be appreciated.
12. Results. “sensitivity and specificity” issues. I would agree with the authors, with the table unchanged, still a commentary should be added. In spite of the fact that these terms have been used in the papers by Zamboni and Zivadinov, there have been already much misunderstanding and controversies associated with the use of such a statistics. In general, from statistical and semantic point of view the terms are not appropriate (the diagnosis of MS is not a gold standard test to diagnose CCSVI !). In addition, taking into account high prevalence of CCSVI in
MS patients, standard statistics should be used with caution and a Bayesian approach seems more appropriate (just a comment).

13. Discussion. Congenital nature of CCSVI. The authors should present alternative explanations of higher prevalence of CCSVI in older patients, as suggested in the previous review. Also, suggested references should be included and commented. It is not appropriate to discuss only the research that is in line with the beliefs of the authors and to ignore those revealing quite the contrary.

14. Discussion. The authors have found that p value for correlation between the age and presence of CCSVI in the controls was 0.635. It is clearly showing that actually no correlation has been found. Consequently, the authors should not claim for such a correlation in the discussion (perhaps, a correlation coefficient should be given, but such thing as “power=30%,” without statistic method used, is highly confusing. Moreover, if CCSVI were simply caused by MS (irrespective of the mechanism responsible), one should expect a positive correlation between duration of MS and CCSVI prevalence, which has not been found by the authors.

15. Discussion. The part “In native vessels...durability” should be deleted. It deals with pathology and physiology of arteries and heart, and should not be extrapolated to the veins. Venous physiology and biophysics is very different from that seen in the arteries.

16. Reference 37. It deals with heart valve pathology. The vein and the heart are two very different things, and the same applies to heart valves and venous valves.

17. English has been improved, but there are still parts of the text written in poor English

**Level of interest:** An exceptional article

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

Potential conflict of interest has been declared in previous review of this paper.