Reviewer's report

Title: Clinical correlates of grey matter pathology in multiple sclerosis.

Version: 2 Date: 13 December 2011

Reviewer: Declan Chard

Reviewer's report:

This revised submission reasonably addresses my previous points. There are still a few points that should be considered some more, to ensure that the intended meaning is conveyed clearly, and some areas where there is perhaps insufficient evidence to make firm assertions. More specifically:

1. Abstract, line 6, ‘correlate well’ - this is a subjective statement, and measures have demonstrated variable associations, perhaps reconsider this.

2. Abstract, last sentence, I am not sure that we can be certain of this. This may reflect the difficulty we have observing grey matter lesions and recognising the clinical correlates of acute cortical dysfunction. Please reconsider this.

3. Introduction, paragraph 1, line 9 - I think this work highlights an important role for immune mechanisms, but has yet to establish causality, please reconsider the phrasing of this sentence.

4. Introduction, paragraph 2, line 3, ‘important … learn to predict’: should this read ‘are able to predict’ or similar?

5. Introduction, paragraph 2, line 11, ‘clinical and cognitive’ perhaps should read ‘physical and cognitive’ or similar.

6. Assessing grey matter pathology, paragraph 1, line 3, ‘together with its reorganisation’ - I am not sure that I follow this, how is atrophy linked with cortical reorganisation?

7. Assessing grey matter pathology, last paragraph, final sentence ‘temporal’ should this read ‘time’?

8. Physical disability, GM atrophy - it would be useful to quote here some of the correlation coefficients, as this will give the reader an idea of the strength of association. I do no think the term ‘closely’ conveys this optimally.

9. Physical disability, GM atrophy - it is noted that not all studies find an association, but this may relate to differences in the cohorts, for example early compared with more established MS, or different subtypes, and this should perhaps be mentioned here.

10. Physical disability, GM reorganisation, first sentence, ‘reorganisation of the GM’ should this read ‘adaptation of neural networks’ or similar? Also, it is difficult to be certain how much reconfiguration of neural networks translates into reduced physical or cognitive deficits, so perhaps reconsider the term ‘principal’ here.
11. Physical disability, GM reorganisation, last sentence, ‘regeneration’, please clarify what is meant by this. Does in mean remyelination, or regrowth of damaged axons and dendrites, or something else?

12. Physical disability, evaluation of disability, line 5 ‘This is probably …’, please provide a supporting reference for this.

13. Cognitive impairment, regional GM changes: while there is less evidence for GM lesions influencing outcomes, it may be worth mentioning here that GM lesions are still more difficult to detect in vivo than are WM lesions.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests related to this manuscript.