Reviewer's report

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

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Reviewer: Declan Chard

Reviewer's report:

I thought the subject of this review interesting, and the literature assessment relatively comprehensive, offering a useful introduction to the field. However, I am not sure that the material quite fits with the article types accepted by the journal, as it does not appear to be a research or debate article (hence the level of interest score). However, if review papers are acceptable to the journal, I believe that it would benefit from some restructuring and refocusing, and the addition of some tables summarising the state of the literature to date.

1. An expanded opening section on histopathology may help set the scene for the subsequent discussion about MRI.

2. Assessing grey matter pathology. This section covers a lot of material and may perhaps be broken down further, for example into lesion and normal-appearing MRI findings. It would perhaps be useful to review all the MRI techniques used in the study of GM, their strength and weaknesses. Also, for the most frequently used methods, such as measures of atrophy and lesion counts, a couple of tables summarising the results of all the available studies would be of interest (including the magnitude of disease effects and strengths of correlations with clinical measures where available).

3. Clinical correlates of GM impairment. This section may also benefit from subdivision and expansion. Which measures are most correlated with MRI measures? The addition of a table summarising studies, the main measures assessed and their correlations with MRI measures, would be interesting too.

4. GM impairment: marker and predictor. The title does not appear to entirely fit with the subsequent material, and perhaps should be modified. Also, it may be worthwhile having subsections on diagnosis, prognosis and surrogate markers separately.

5. Conclusion. Maybe include something on areas for further research attention. Also, the comment on the use of GM measures as markers for the effectiveness of current immunomodulatory therapy is interesting, and could be developed as a sub-section in the body of the review. Lastly, I am not sure that the GM per se is a target for therapy, rather pathology in the GM may be. Some pathological processes may be more apparent in GM than WM, for example neurodegeneration, and so measures assessing this in GM may be more sensitive to treatment effects than those in WM.

Level of interest: An article of limited interest
Quality of written English: Acceptable

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.