Reviewer's report

Title: Tract integrity in Amyotrophic lateral sclerosis: 6-month evaluation using MR diffusion tensor imaging.

Version: 0 Date: 10 Aug 2018

Reviewer: Francesca Trojsi

Reviewer's report:

Alruwaili et al. aimed to investigate significant longitudinal changes of Diffusion Tensor Imaging (DTI) measures across 6 months. The authors revealed that both voxelwise TBSS and ROI analyses did not show significant differences between the two scans in FA and MD measures. No significant correlations were revealed between FA or MD and ALSFRS-R at the two timepoints and across time.

The paper is well written and articulated as a short report. However, some limitations of the study, also accounted by the authors, have been linked to the relatively small sample of patients, the inclusion of patients with slow progression and the relatively short interval between scans.

1) In the abstract the authors specified that this study aimed "to assess changes in diffusion tensor imaging (DTI) over time in patients with amyotrophic lateral sclerosis (ALS), to see if this is a biomarker of progression". However, the study design did not allow to establish if changes in DTI measures over time may represent potential biomarkers of progression in ALS (i.e., needing larger datasets, longer follow-up timeframes, and multimodal approaches). Please attenuate this statement.

2) Some patients exhibited a slow progression. Please refer in the "patients and methods" section the clinical ALS phenotypes included (according to Chiò et al., J Neurol Neurosurg Psychiatry 2011; 82:740-6; i.e., classic, bulbar, flail arm, flail leg, pyramidal, respiratory, pure lower motor neuron and pure upper motor neuron phenotypes).

3) The radial and axial diffusivity (RD, AD) measures were not reported. Were not significantly different by comparing the two scans of this patients sample? Although less frequently explored, some recent evidence revealed changes of RD and AD across time in some ALS cohorts of patients (de Albuquerque et al., NeuroImage: Clinical 2017:14;269-276; Menke et al., NeuroImage: Clinical 2018:17;953-961). Please address this issue and show and discuss RD and AD changes across time in this ALS population.

4) The conclusions may be more integrated by reporting that the lack of significant changes in DTI measures across time may be due to the evidence that white matter is already substantially damaged by the time of onset of symptoms of ALS.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable
Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.