Reviewer’s report

Title: Machine Learning Analysis of Motor Evoked Potential Time Series to Predict Disability Progression in Multiple Sclerosis

Version: 1 Date: 22 Sep 2019

Reviewer: Manuel Vázquez-Marrufo

Reviewer's report:

The main goal of the manuscript is to perform machine learning analysis of motor EP (using whole series - raw data) instead of a few variables (latency, morphology, etc) to predict disability progression. This kind of application is interesting and has been developed in different ways and with different type of variables.

However, my suggestion after reviewing the manuscript is that it needs a major revision before publication. My main concerns are listed below:

1) There is not a clear description about the way to export the raw series for the EPTS. Particularly important is the difference that could happen in any particular patient considering the demielinization process that is usually present in these patients. I would suggest a table where it would be indicated the latency as a reference for exportation of data and for any particular subject. Later, indicate the precise interval that is used for calculations and describe the size (in time) and why that selection.

2) Probably the main concern in this study is the "noise" contribution to the raw data and the way that it affects to the operation of the machine learning processing. Indeed, authors indicate in the text (page 27, line 23), that improving the prediction of disability results quite difficult due to the noise of data. I strongly suggest calculating and indicating the signal-noise ratio in the intervals used for the calculations. In this case, a figure with a grand average of EP will also help to figure out how "clean" are the general or individual EPs.

3) A more general concern refers to the application of the manuscript in the clinical field. After reading it, it looks specially focused in the algorithms used more than in the impact for the neurology of these patients. A more detailed discussion about the contribution to the evaluation or potential applications in the neurology field would be recommendable.

4) Lastly, and considering that it looks that the authors dispose of a wide clinical data from patients, it would be recommendable to improve prediction of evolution with a more general view of the disease and consequently variables included (structural, biochemical, physiological, etc) to make a more striking contribution of prediction in Multiple Sclerosis Disease. Indeed, this is one of the conclusions from the authors in the conclusion section.

As minor points:

*) The number of references is somehow unbalanced when reviewing contributions in the use of EPs in Multiple Sclerosis (page 3, line 30).
Aside from the comment of discussion above, this section looks somehow disorganized and not easy to read.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Unable to assess

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

No

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

No

**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 recommend additional statistical review

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

Acceptable

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