Reviewer’s report

Title: Quantitative electroencephalography reveals different physiological profiles between benign and remitting-relapsing multiple sclerosis patients

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Reviewer: Letizia Leocani

Reviewer’s report:

Comments to manuscript: Quantitative electroencephalography reveals different physiological profiles between benign and remitting-relapsing multiple sclerosis patients by Manuel Vazquez-Marrufo et al.

1. Is the question posed by the authors well defined? Yes
2. Are the methods appropriate and well described? Yes
3. Are the data sound? Yes
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes
5. Are the discussion and conclusions well balanced and adequately supported by the data? No, there is an issue that should be considered on the finding on increased beta and gamma power in MS patients, since a higher contamination by electromyographic activity cannot be excluded.
6. Are limitations of the work clearly stated? No (for the reason in point 5)
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes
8. Do the title and abstract accurately convey what has been found? Yes
9. Is the writing acceptable? Yes

Reviewer’s report

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- Major Compulsory Revisions

In this study, increased right frontal (F4) and bilateral occipital (O1 and O2) beta and gamma bands at Q-EEG (absolute power) have been found in the preparation period of the Posner cued visual reaction time paradigm, in a group of RR MS patients but not in benign MS patients when compared with a control group of healthy subjects. Although the authors correctly address possible confounding sources for such finding (e.g. ocular artifacts which should have been bilateral, higher anxiety level, preexisting use of psychoactive drugs) another source of confounding is a possible higher artifactual contamination by muscle activity in MS patients compared with control subjects. The fact that significant findings were obtained only in F4 and not in F3 is not possible to interpret since the values from F3 are not shown (not being significant),
preventing a comparison of the magnitude of the effect over the right hemisphere compared with the left (in Table 2, the p value for F4 post-hoc in RR vs controls ranges from 0.02 to 0.04, not much above the limit of significance). Moreover, the study investigated absolute power (an increase, in RR patients, of beta/gamma relative power only, with no difference in absolute power, would have been a stronger finding in favour of a shift of brain oscillations towards higher frequencies and not just an increased amount of high-frequency power which could be artifactual). Moreover, EEG was analyzed during the 512 msec prior to the imperative stimulus, and no comparison was performed with baseline in order to assess whether this beta/gamma power increase in RR vs controls was task related or was preexisting (in the latter case, the need for a compensatory mechanism in interpreting this finding would become weaker). In fact, as the authors point out, ‘This study has shown that QEEG scores do not correlate with the cognitive impairment which indicates a relative independence of both variables as has been described in other studies… The lack of correlation between QEEG scores and cognitive impairment does not mean a complete independence between these two processes. An increment in the high band QEEG scores could be an alerting signal to activate compensatory mechanisms that of course will help in the cognitive performance of the subject.’. Such interpretation should rely on the exclusion that such differences in RR patients compared with controls are not related to EMG artifacts escaping visual inspection, and are not already present at rest. Therefore, data showing that differences between RR and controls are related to the task and not present at rest (from resting EEG in the same patients or at least the baseline period prior to the cue), should be provided. In case this is not possible, the issue of both EMG contamination and of preexisting differences in brain oscillations should at least be addressed in the discussion.

- Minor Essential Revisions

Data from F3 should be indicated in Table 2: although non significant, they would help the reader in comparing the magnitude of the significant effects in F4.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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