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

Authors:

Manuel Vazquez-Marrufo (marrufo@us.es)
Javier J Gonzalez-Rosa (javgonros@us.es)
Encarnación Vaquero (evaquero@us.es)
Pablo Duque (pablo.duque.sanjuan@gmail.com)
Monica Borges (monica.borges@neuroinvest.net)
Carlos Gomez (cgomez@us.es)
Guillermo Izquierdo (ayuso@arrakis.es)

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Author's response to reviews: see over
Dear Editor-in-Chief:

We are attaching a revised copy of the manuscript titled “Quantitative EEG reveals different physiological profiles between benign and remitting-relapsing multiple sclerosis patients” by M. Vázquez-Marrufo, JJ González-Rosa, E. Vaquero, P. Duque, M. Borges, C. Gómez and G. Izquierdo which we would like to submit for publication in BMC Neurology.

As recommended by the editorial policy, we include a point-by-point response to the concerns:

Reviewer #1

Artefact contamination by muscle activity.

We agree that such activity could represent a threat to our data. One possible way to disregard it is based on the same reasoning used about other variables such as anxiety or motivation levels. It looks unlikely that only RRMS patients showed an artefact contamination and no one from the BMS and control group exhibited it (see patient by patient data, table 3). But this theoretical reason is based only on probability. To answer this question empirically, we have calculated ERPs for the same intervals and trials where spectral analysis was performed. This checks possible muscle artefacts in the RRMS patients compared to BMS and control group. The figure shows that there are not any evident muscle activities between groups (see new figure 2). Another possibility for artefact contamination could be produced by the effect of tension in neck muscles. We have tested T5 and T6 (that usually exhibits muscle activity in the neck area) and we found no differences in these bands in the experimental groups. Stats Results: Beta-2 [F(2,47)=1.368, p=0.264]; Gamma [F(2,47)=1.495, p=0.235].

We include the figure of CNV and the commentary about this issue in the discussion section.

F3 Values are not shown.

We have included these values in the table 2 and show that there are no significant differences in F3 electrode comparing groups (which are always over 0.1). In any case, we do not assert in the manuscript that this asymmetry (F3-F4) has any special interpretation. We consider that new studies are necessary to confirm this topography (right for frontal and bilateral in the occipital area).
The use of absolute spectra instead of relative power.

The use of relative power is not always the best choice. In some cases, modulations show in all bands in the same way (a general increase) and the result of relative analysis will show no changes in the spectral content -what is not a complete view-. However, it looks that the threat of muscle artefacts can be ruled out in our data.

Comparison with baseline.

Again we agree. We performed another analysis to check if the increase of beta and gamma bands were present even without any cognitive tasks. The result of the analysis showed that there are no differences in the gamma and beta-2 bands in periods of resting (analysed in the pause intervals between blocks) among RRMS patients and BMS or control subjects. We can conclude that it is necessary that the subject performs a cognitive task to show an increase in these bands. At least in this particular case. Stats Results: Beta-2 [F (2,47)=0.505, p=0.607]; Gamma [F (2,47)=0.729, p=0.488].

We have considered that the best way to include this comment is an explanation in the text as recommended by one of the referees.

The lack of correlation does not mean a complete independence between these two processes.

This is also our point of view. Indeed, in the sentence that the referee highlights from our manuscript, we indicate that there is a “relative” independence not a complete one. The following reasoning from the referee “An increment in the high band QEEG scores could be an alerting signal to compensatory mechanisms that of course will help in the cognitive performance of the subject” is precisely our interpretation of our data. But the compensatory mechanisms could be directly related with the cognitive process under study (visual-spatial tasks) or more related with general mechanisms like alerting. This is something to be analysed in next studies.

Minor essential revisions (include F3 values in table 2).

They have been included as described above.

Reviewer #2

The lack of correlation with MRI features.

This is a good point from the referee. After to the results in this manuscript, we propose a further study including subjects with a MRI exploration. We will include different forms of Multiple Sclerosis (the primary progressive form, where our hypothesis can be checked). Where the comment is relevant, it has been included in this revised version of the manuscript.

The paper is too long.

We have calculated that our present manuscript is quite similar in length to our previous study published in BMC Neuroscience. However, we have reviewed the manuscript and
find some paragraphs that could be omitted (mainly of examples). References have been also reduced in number because of the reduction of these paragraphs. Also the old figure 1 has been removed as recommended by the referee.

**Figure 1 should be omitted.**

It is true that information provided in the text makes the figure unnecessary. We included it in the first version because we believe a figure clarifies the absence of the speed-accuracy trade off. To shorten the manuscript we have removed this figure in the revised copy.

**The manuscript should be edited for fluency in English.**

We have employed an external copyediting service.

Kind regards  
Yours sincerely,

Dr. Vázquez-Marrufo  
Laboratory of Psychophysiology  
Department of Experimental Psychology  
University of Seville  
Camilo Jose Cela s/n  
41018  
Seville  
SPAIN  
Marrufo@us.es