Reviewer's report

Title: Exploring the predictive value of the EP score in Multiple Sclerosis within an appropriate dataset: a hint for an early identification of benign MS?

Version: 1 Date: 27 April 2012

Reviewer: Jolijn Kragt

Reviewer's report:

Review manuscript BMC Neurology
Margaretella et al, Exploring the predictive value of the EP score in Multiple Sclerosis within an appropriate dataset: a hint for an early identification of benign MS?

The goal of this study was to evaluate the predictive value of an Evoked Potential (EP) score in MS patients by determining how an appropriate dataset should be defined, and to assess the performance of a logistic regression model based on data collected at the time of the first neurophysiologic and clinical examinations.

The fact that MS is such an unpredictable disease is for patients as well as medical doctors a difficult issue to cope with. To give a detailed prognosis on how disability will develop in the disease course is hardly impossible. Every method that will reduce this uncertainty is most welcome. Therefore, the examination of the ability of the EP score to predict disease progression in MS is interesting and valuable.

However, although the data collected for this study have the potential to answer many different research questions, there are some major issues that need to be addressed.

Major compulsory revisions:
1. In the title, I would suggest to avoid abbreviations. Therefore, change ‘EP’ to ‘Evoked Potential’. On the other hand, MS is such a widely known abbreviation that it is not necessary to write ‘multiple sclerosis’.
2. In the Abstract, Methods and Results should be divided into two separate sections.
3. In the Background section, the before last sentence (beginning with ‘The definition of …’) needs to be explained. Maybe, giving an example would be informative. Furthermore, would it be better to use ‘patient population’ instead of ‘dataset’?
4. In the Background section, the aim of the study requires to be explained elaborately. For instance, why are EP scores necessary to use in MS? Why this study is interesting next to what has already been published on this topic? Besides, the second part of the sentence on the aim of the study is not clear to me at all; what do the authors mean by this model? Perhaps, you could
emphasize on the importance of the study results for benign MS.
5. In my opinion, the Methods section needs to be placed before the Results section.
6. In the Results section, the model is validated on new data. However, this ‘new’ patient population contains 11 ‘old’ patients. It would be better to remove these 11 patients from the analyses.
7. In the first paragraph of the Discussion section, ‘4’ EP modalities should be changed to ‘5’ EP modalities, and figure ‘6’ should be changed to figure ‘5’.
8. In the second paragraph of the Discussion section, results of different studies are combined and shown in one figure. In my opinion, this should only be done in extensive meta-analyses.
9. In the second paragraph of the Discussion section, reference 15 is a study on ALS patients. This is probably a mistake?
10. In the Patients part of the Methods section, the time to reach EDSS 2.0 is introduced as a variable. How can you compute this variable when you only have two EDSS assessments (EDSS at first and EDSS at final time point)? The EDSS at the final time point is already being used as outcome variable.
11. Please explain in the EP score part of the Methods section how the score has been calculated. Is it a summary score?
12. The reference section needs to be updated.
13. Clarify in the Statistics part of the Methods section why the threshold of EDSS 3.5 is interesting clinically. Why the widely used definition of clinically significant change on EDSS (>= 1.0) has not been applied?

Minor essential revisions:
1. In the Background section of the Abstract, change ‘confound’ to ‘confounding’.
2. In the Background section of the Abstract, explain ‘NE’.
3. In Background, explain ‘EPs’.
4. In Background, change ‘connected’ to ‘confined’.
5. In Background, explain ‘NE’.
6. In the fourth paragraph of the Discussion section, ‘mean’ EDSS should be ‘median’ EDSS.
7. Figure 1 might need more explanation/clarification. For example, what is the model predicting?
8. In figure 3, add ‘curve A’ and ‘curve B’.
9. In figure 4, add ‘curve C’ and ‘curve D’.

Discretionary revisions:
1. In the Results section, the correlations might be classified as weak-moderate-strong.
2. In the Results section, linear regression would be a better way to examine the
influence of possible confounding factors, instead of stratifying the patient population.

3. Concerning Table 2, it would be interesting to show the EP scores and disease duration for the two EDSS groups in the upper part of the table.

4. The formula in the Results Section is not informative to the reader. It would be far more interesting to explain what this model might tell us.

5. You might decide to remove Figure 1 from the manuscript.

6. The Discussion section would become more comprehensible starting the section with a summary of the most important results and then discuss the findings.

7. Figures do not belong to the Discussion section.

8. In the fourth paragraph of the Discussion section, the relevance of the EP score is being discussed. The findings that the EP score is relevant in a group of patients without much clinical damage (low EP score) and simultaneously is relevant in a group of patients who are worsening rapidly (TT2 <= 3 years) seem contradictory to me. You might elaborate more extensively on this theme.

9. For discussion: to compare predicting variables, likelihood ratios are suitable. To calculate these ratios would improve the manuscript significantly.

10. How would choosing a new end point (e.g. EDSS 6.0) affect the predictive abilities of the EP score?

11. The article of Kalkers et al on motor evoked potentials (Clin Neurophysiol 2007) might be added to the reference list, for example after number 9.

In conclusion, this manuscript presents some interesting data. However, quite a few major comments need to be addressed before this manuscript might be accepted for publication.

Dr. J.J. Kragt, MD PhD,
Department of Neurology
UMC Utrecht,
The Netherlands.

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.