Reviewer's report

Title: Stable cognitive performance in relapsing remitting multiple sclerosis patients during 2 years treatment with intramuscular interferon-beta-1a: an observational study in daily practice

Version: 2 Date: 9 January 2011

Reviewer: Richard Benedict

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Review of “Stable cognitive performance in relapsing remitting multiple sclerosis patients during 2 years treatment with intramuscular interferon-beta-1a: an observational study in daily practice” Jongen et al

It is a pleasure to read this manuscript on an important topic in MS research.

ABSTRACT

In the Abstract and throughout the manuscript, the term “information processing” should be further qualified – all cognition involves the processing of information.

The term “Power of attention” etc, should be defined. Are these psychometric tests? If so they should be capitalized as other proper nouns.

As there is no control group, the authors should not offer conclusions about the effects of treatment on cognition.

INTRODUCTION

More robust correlation is found between cognitive function and whole brain and regional gray matter atrophy, rather than lesion volume. The literature review should reflect this.

The authors should acknowledge that other DMTs also reduce MRI lesion load and relapse rate.

The term “real life” is vague and depending on what the authors are trying to convey, the point may be irrelevant.

As there is no control group, the study was not designed to investigate “the effectiveness of IM INF#-1a in postponing cognitive decline in RRMS patients treated in daily practice.”

The authors note that “three of the MACFIMS tests (D-KEFS sorting, 10/36 and especially BVMTR) are dependent on complex motor responding.” This is false – the motor responding is simple – for example, on DKEFS subjects only move cards around.
At the bottom of page 5, DSST is not defined. It is later but not referenced. Why did the authors use this test, which to my knowledge has not been validated in MS?

At the point of introducing the CDR, a new paragraph should be designated.

Please explain how information is “recalled” on this computer administered test – I believe this is probably a recognition memory task. Please reference data that shows the alternate forms of CDR are equivalent in difficulty.

METHODS

The DSST is not widely used. The authors may be confused about the difference between SDMT and DSST. Ironically, after criticizing other tests from MACFIMS for reliance on motor function, the authors employ the DSST which requires copying symbols as fast as possible.

The MS54-QoL may be mislabeled. Is this the MSQOL-54? Authors reference #22 but in the bibliography 22 refers to PASAT.

It is not clear how the various indices from the CDR are calculated for example “power of attention” or whatever that may be.

The analysis does not model treatment effects as there is no control group. The ANOVA is not a mixed model, as there is no between-groups effect. There is no reason to include age as a covariate. The rationale for selecting the identified pairings with t tests is not explained. The best approach is to examine the effects of the model and then examine simple effects is the general effect is significant. The general effect should include all time points.

It is not valid to arbitrarily select cases from another database which is not even peer-reviewed and then use the data as a control group.

I believe there is a typo, a Bonferroni correction would not be p=0.05.

RESULTS

The test-retest correlations are of interest, but all time points should be included. This would be a better study if it were focused exclusively on the reliability of CDR in MS.

Cronbach’s alpha is not a measure of “stability.” Its use in this context is not clear.

The entire ANOVA model is never presented.

DISCUSSION

There is no basis for concluding that medication had any influence on cognition in this study.
Level of interest: An article of limited interest

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