Reviewer's report

Title: Low contrast visual acuity testing is associated with cognitive performance in multiple sclerosis: a cross-sectional pilot study

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Reviewer: Ralph Benedict

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This is a well written manuscript that reveals significant correlation between low contrast visual acuity and neuropsychological testing in MS. A few other groups have reported on the same association, interpreting their findings as showing a confound between visual acuity and cognitive performance. This study is unique in that the design includes OCT. The sample size is also an asset for this study.

The abstract highlights SDMT and PASAT and does not report that the entire BRNB was administered.

Throughout I find errors regarding the manner in which psychological constructs are defined. The BRNB does not include a test of sustained attention [eg continuous performance test] or focused attention for that matter. The use of the term ‘attention’ is not correct, and it matters not because in contrast to the manuscript there is little evidence that MS patients suffer from disordered attention. They do have impairment in processing speed and working memory.

The authors acknowledge at the end of the Discussion that the data are cross-sectional and offer no inferences regarding causality. Yet the manuscript is littered with suggestions of causal effects. For example, in the Abstract, “our data show that cognitive impairment potentially diminishes performance.” To begin with, their data could just as easily be interpreted as showing that poor visual acuity impacts cognitive performance, rather than the other way around.

Second paragraph of Introduction, first sentence, there is a missing word at the end of the sentence.

A methodological weakness is failure to exclude patients with other causes of cognitive impairment, including psychiatric illness.

On page 5, all of the cognitive tests should be referenced.

From the outset the BRNB z score is not defined. Is this a composite z score? In the analysis section only the PASAT and SDMT are discussed whereas all of the tests in the BRNB were analyzed.

In Table 2 and throughout the Results please present all of the standardized betas and the r values so that the reader can judge the effect sizes across all metrics.
The authors point out that this is preliminary work conducted with a sample that is not very impaired compared to other studies. It is premature to present cut scores that could easily be misapplied in clinical work with patients. I think this part of the paper should be deleted altogether. Furthermore, I do not know what a ‘local regression analysis’ is.

The authors may be interested to know that LCVA and SDMT are proposed metrics for a revised MSFC as noted in recent task force meetings on this very topic [Cohen et al. Lancet; Ontenada et al. MSJ].

I am puzzled about one aspect of these findings. The authors argue that since RNFL was controlled for and there still is a relationship between various tests and LCVA, that means that cognitive ability is involved in the LCVA metric. They sometimes refer to these outcomes as complicated or complex visual tests. What is complicated about them? Sure, the stimuli are harder to see than with a Snellen chart, but it is still a task of look at the board and tell us what you see. What is complicated about that? Moreover, how do you explain that memory tests are related to these outcomes – surely no memory performance is required? I think there is an inferential error. The authors claim that overall disease burden is controlled by including RNFL in the model, but OCT-RNFL is NOT a proxy for overall disease burden. EDSS or MRI BPF would be closer to this idea.

In the Discussion, these small effects, for example $r = 0.34$, are described as closely linked or strongly correlated, which of course is not true. EDSS correlates at this level with cognitive function. Do we then conclude that physical disability is closely linked with cognitive dysfunction?

Overall a good paper, but the inferential leaps need to be curtailed.

**Level of interest:** An article of importance in its field

**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' below