Reviewer’s report

Title: Quantifying cognition at the bedside: A novel approach combining cognitive symptoms and signs in HIV

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Reviewer: Carolyn Fredericks

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The authors use Rasch measurement theory to combine items from the MOCA, a computerized cognitive battery, and patient self-report (PDQ) in an effort to (1) show that self-reported symptoms are part of the same global cognitive performance construct as cognitive testing outcome measures and (2) provide a new, short battery that will be sensitive to very early / mild cognitive changes in individuals with HIV. The need for a shorter, validated measure of mild cognitive changes in HIV is fairly well-motivated and the manuscript is well-written.

To strengthen the manuscript, I have the following recommendations:

* The authors state in their introduction that "interventions may be more likely to succeed at earlier stages of [cognitive] impairment." To better motivate the need for early screening and identification, please clarify which interventions, and provide citations. Similarly, please clarify the limitations of existing screening tools (currently described simply as "poorly targeted") — are these only valid for a greater degree of impairment?

* Relatedly, in terms of the need for tools to validate cognitive complaints, as the authors point out in their discussion, there is already evidence linking self-reported cognitive complaints with objective assessment of everyday function in this patient population. What does this work add from the clinician's perspective?

* The authors state that a "systems" approach to neuropsychological testing "may be less appropriate in HIV, where deficits likely arise from diffuse network degradation rather than the focal cortical or hippocampal degeneration seen in many primary neurological disorders." Most neurodegenerative disorders are associated with disruptions in specific networks rather than focal degeneration (Seeley 2009, Neuron). Some degenerative disorders, including vascular dementia, chronic traumatic encephalopathy, and others, can show similar cognitive deficits to those described in HIV (attention, executive function, processing speed). The authors should clarify what makes HIV cognitive impairment special and why it is appropriate to measure cognitive function as a single construct in this disorder, as opposed to other disorders.

* In referring to their prior work with Rasch models for MOCA items in HIV, the authors state that "these items alone were too easy to precisely measure the two samples we studied." Please clarify what is meant by "too easy" — was there a ceiling effect? What exactly was disappointing about the MOCA results that motivated the present study?
* In the Methods section, please provide a citation for "recommended steps with the RUMM2030 software."

* As the data from computerized items and self-report items are added to the Rasch model, the p-value for global fit gets smaller, approaching the 0.05 threshold at which the Rasch model would be rejected — though internal reliability/PSI improves. For readers less familiar with this statistical approach, authors may want to touch on this aspect of fitting the model. Should readers focus only on the measure of internal reliability?

* The single outlier participant is described as having "likely cultural and educational differences" — is he or she an outlier in terms of years of education or other standardized measures that were collected?

* In the results section, the authors state that "three-quarters of this sample met criteria for depression," but in Table 1 only 37% do. Please clarify.

* The implications of a large percentage of participants meeting criteria for depression are very important here, especially as authors describe depression being a major confound for clinicians confronted with patients with mild cognitive complaints, and prior reports have shown that self-reported cognitive symptoms correlate highly with depressive symptoms and not as well with objective task measures (cited in Valcour 2011). Depression in itself could certainly contribute to impaired attention and cognitive slowing. Does subgroup analysis show that the non-depressed patients perform similarly to depressed patients? Does the model hold in both cases?

* The authors identify the need for a shorter, more economical alternative to full neuropsychological testing in this population and include a battery of computerized tests in their assessment, with which they hope to capture subtler cognitive impairment than can be seen on the MOCA. However, details on which computerized tasks remained in the model and how participants performed, compared with healthy controls, are not included. This will be important to readers' understanding of what the computerized tasks add to the MOCA.

* Table 4 is difficult to interpret, especially since we don't know what the individual computerized tasks were; labels for tests other than the PDQ items are difficult to interpret, and it's hard to tell MOCA from computerized items at a glance. Recommend highlighting items from different groups in different colors.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No
Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes

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