Author's response to reviews

Title: Pattern of neuropsychological performance among HIV positive patients in Uganda

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Author's response to reviews: see over
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Re MS: 1934453505115295
Pattern of neuropsychological performance among HIV positive patients in Uganda Kevin Robertson, Noeline Nakasujja, Matthew Wong, Seggane Musisi, Ellie Katabira, Thomas Parsons, Allan Ronald and Ned Sacktor

Dear Editors:

Please accept our revisions to the manuscript entitled ‘Pattern of neuropsychological performance among HIV positive patients in Uganda’. Please see an itemized list of our revisions below. We want to thank the reviewers for their work in making the manuscript much improved.

Sincerely,

Kevin Robertson, Ph.D.
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Reviewer 1.
Major:
1. The abstract notes that the group differences were largely driven by HIV-positive individuals with WHO stage 4 disease. I didn’t see these results laid out in the results section of the paper. The authors are encouraged to describe these results in the body of the paper.

Response: I have corrected the abstract. The correlations for WHO disease stage are in the results sections.

2. It appears that the two groups of participants differed notably on education (mean of 9.1 vs mean of 12.0). The authors should consider correlational analyses to determine whether education is related to neuropsychological performances and if so, run ANCOVAs with education as the covariate.

Response: We ran the correlation as noted above by the reviewer, and there was a correlation between years of education with many of the tests, but not with age. ANCOVA’s were run and the results have been updated in the text. The table presents the raw unadjusted means and standard deviations and remains the same.
3. The authors are encouraged to discuss their findings in the context of other recent international studies of nonclade B HIV (e.g., Yepthomi et al, 2006, JINS).

Response: We incorporated a discussion of the Yepthomi reference into the manuscript.

Minor:

1. Were all HIV-positive individuals treatment naïve?

Response: No, 49 of 110 had some prior antiretroviral treatment with varying regimens. This was added to the text.

2. The WHO neuropsychological battery has been administered in multiple countries and it may be useful to inform the reader whether the battery has been administered in Uganda and translated into Luganda. In the event it hasn’t been translated, could the authors comment on whether the items were reviewed for specific utility in this culture.

Response: The battery was translated into Luganda.

3. Could the authors comment on how many individuals were tested in each language (English vs. Luganda) for each group? Did these language groups differ on the tests within and across serostatus?

Response: Formal analyses were completed, no differences were found between main language group, within or across serostatus. Most of the subjects (81% HIV- and 77% HIV+) were tested in Luganda. These has been incorporated into the text.

4. Presumably the specific clade status of individuals in this study was not known. If true, it may be useful to comment in the discussion as to whether the authors would predict any differences in cognitive outcome between these two clades.

Response: This is a good point, Layendecker found clade A had faster systemic progression over clade D and we have commented on this in the text of the discussion.

Reviewer 2:

Major:

1.) Although the topic of this study is important, the authors need to take the time and care to present a clear, thoughtful, and organized manuscript. Terms, concepts, citations, grammar, and language in general need to be carefully employed here. The authors also need to take the time to cite more relevant studies from the extensive literature on neuropsychology of HIV/AIDS and relate them to their findings. More focus and care will improve this manuscript greatly. Below are several comments to assist the authors.

Response: We generally agree, have cleaned up the manuscript throughout, and address specific points requested by the reviewer below.
2. In the Abstract, the authors state that post hoc analyses were conducted to compare neuropsychological performance among WHO stages in the HIV+ adults. However, in the Results section of the manuscript it appears that post hoc analyses were conducted not on WHO groups but on MSK groups. This needs to be clarified.

Response: This was also noted by Reviewer 1, and the abstract has been corrected.

3. On p. 5 at the end of the Introduction section, the authors state that the purpose of the study is to evaluate neuropsychological performance in HIV+ patients. However, much of the preceding discussion in this section focuses on HIV associated dementia (HAD). A LOT of research has been conducted on the neuropsychology of HIV without explicitly looking at dementia (which is the purpose of the present study)—studies looking at attention, working memory, learning and memory retention, executive functioning, information processing, etc.—but most of this literature is completely ignored in the Introduction. This omission is rather unusual.

Response: We agree that there is an extensive literature on the neuropsychology of HIV and chose not to review this given that this would require an extensive review. Nevertheless, we have revised this section.

4. To be quite frank, the statistical results are presented sloppily. First of all, in the subsection “Data Analytic Plan”, they refer to analyses based on MSK rating but not on WHO stage. Analyses were done on both grouping variables (I’m not entirely sure why) and this needs to be stated in this section.

Response: We agree, and have cleaned up the analyses. We present analyses of the MSK rating to address dementia staging, and the WHO stage analyses to address systemic disease.

5. In the Results section, I’m not sure what they are referring to when at the very beginning they discuss a difference in “neuropsychological total z-score”. They don’t appear to combine all test scores into a single z score. They refer the reader to Table 1 but I don’t see it their (they also refer the reader to a non-existent figure?).

Response: We agree that reference to Table 1 was misplaced, and the reference to the figure that was removed has been corrected in the text. The methods section noted a total z score.

6. Table 1 itself needs to be cleaned up. The line spacing is not uniform, results need to be lined-up with the test heading, group headings should be centered, and so on. Also, abbreviations for test names are difference between Table 1 and Table 2. These obviously need to be uniform.

Response: We agree, the tables have been cleaned up.

7. In addition, the group headings on Table 2 are not uniform (the .5 group is placed on two lines while the 0 and 1 groups are on one line) and they don’t match the group names in the text. Table 3 has similar problems with uniformity. The authors need to take the time to re-work and clean-up these tables.

Response: We agree and have cleaned Table 2. Table 3 appeared superfluous and has been deleted.

8. For the text in the Results section, statistical results need to be presented in a standard fashion. For many of the ANOVAs, degrees of freedom are not presented. Perhaps the authors were trying to save space or be economical in presentation style. Nonetheless, results need to be uniform. Perhaps they could present ANOVAs in a table? Same issue applies to the series of correlations they conducted.
Response: We agree, and have added the F values to the table, and generally cleaned the statistical presentation up.

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Minor Revisions:
In the Abstract, groups based on WHO stage is mentioned. But subjects were also analyzed by MSK rating, so this should be mentioned as well.

Response: The abstract has been revised.

On p. 4 (second paragraph, second line) the term “HIV dementia” is used. Since they use the term minor cognitive motor dysfunction (MCMD), the authors might as well use a more concrete term like HIV associated dementia (HAD) or some other standard term. The same issue exists on p. 5 (line 2), where the term “HIV Dementia” is used. Dementia does not need to be capitalized, and they might as well use the term “HIV associated dementia, etc.

Response: We agree, and attempted to use consistent terminology where possible. The term AIDS Dementia preceded HIV Associated Dementia or HIV Dementia, and are often used interchangeably, much to the confusion of some readers unfamiliar with the history as the reviewer notes.

On p.4 (second paragraph, last line), the reference they cite [9] after the statement “. . . and difficulty completing instrumental activities of daily living” is incorrect. Navia, Jordan, and Price (1986) do not examine activities of daily living; they present only neurocognitive/neuropathological data on HIV patients.

Response: We agree, this has been corrected.

Authors should strive to be precise in their statements as well as their citations. For instance, on p. 4 (paragraph 3, lines 2-3), they state “HAART can improve cognitive performance in individuals with HIV-associated cognitive impairment . . . “ and they cite two studies by Sactor et al. These studies show improvement only in psychomotor slowing—one specific factor in the spectrum of cognitive functioning. Authors should either talk specifically about psychomotor slowing improvement, or cite other studies (which have been done) that examine cognitive performance (memory, attention, etc.).

Response: This has been addressed in the text, with use of more general terms that subsume both cognitive and psychomotor processes.

The last line on p. 4, the term “clade” does not need to be capitalized.
On p. 6, there should be a colon after the subheading “WHO Disease Staging System”.
On p. 6, subject demographics are presented awkwardly. Perhaps a Table could be used, or at least conventional sentences.

Response: These items have been corrected.

On p. 7 (first paragraph), WHO clinical stages are described as “Stage 1 through Stage 4” but also described as Stage I, Stage II, and so on using Roman numerals. Consistency is obviously needed here. Also, they insert in this paragraph some colons in some very unusual places. Grammar needs to be fixed.
On p. 8 (lines 7-8), they state that “Once the instructions were clear the two groups did not differ in performance.” I don’t know what the authors are referring to.
On p. 9, on lines 2-3 of the Results section, a Figure 1 is mentioned. There is no Figure 1 in the manuscript I reviewed.
Response: These items have been corrected.

On the last line p. 9, a Figure 2 and 3 is mentioned. But in the manuscript I reviewed there are no figures at all.
Two citation conventions are used. Some citations use a number notation but other citations use author names (for example, see p. 7, such as Miller et al., 1990). One citation style, the one appropriate for BMC Neurology, needs to be used.
On p. 7 there is a citation (Miller et al., 1990) that is not included in the reference section.

Response: The citations and items have been fixed.