Author's response to reviews

Title: The Beijing Version of the Montreal Cognitive Assessment as a Brief Screening Tool for Mild Cognitive Impairment: A Community-based Study

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Author's response to reviews: see over
Dear editor,

We are resubmitting our paper entitled “The Beijing Version of the Montreal Cognitive Assessment as a Brief Screening Tool for Mild Cognitive Impairment: A Community-based Study” (MS: 1100918463663332 ) as invited.

Thank you for offering us the opportunity to revise our paper. Your comments and those of the reviewers were very helpful. We have made substantial changes to the manuscript and we now believe it is much improved.

In current version, we detailed the diagnostic criteria of MCI, and added the recently published literature (Lu et al., 2011) and discussed the possible reasons for the divergent results between theirs and ours. Furthermore, based on our findings, we changed the conclusion that the MoCA-BJ is a suitable screening tool for MCI detection in Chinese population to an acceptable screening tool with a few items (constrained by culture, language and education) needed to be modified. We also hav asked a native speaker to assist us with language editing.

Details on the changes are provided below. For clarity, we numbered the reviewers’ comments in the order that they appeared in the review.

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Reviewing 1

1. Although this manuscript asserts in multiple places (p. 6, p. 13) that it is the first to study the utility of the MoCA-BJ in a large community-based cohort, a brief literature search indicates that a much larger (n=8411) multi-center study of the MoCA-BJ that also incorporated rural and urban samples was recently published (Lu et al. J Geriatr Psychiatry Neurol, 2011, 24:184-190). That study, in contrast to the current study, clearly demonstrated the superiority of the MoCA-BJ over the MMSE for distinguishing MCI from normal cognition. The authors should at least acknowledge this earlier study, and consider exploring possible causes for the divergent results. In a similar vein, the authors cite some previous smaller studies with the MoCA-BJ, but do not compare their results to those studies either. Since those papers are only available in Chinese language journals, a more detailed discussion of their results might be useful should the current manuscript be published in an English language journal.
Our Reply:

We appreciate reviewer informing this new publication, which we found also after our original submission.

In this revision, we added this literature in and discussed the divergent results. Basically we proposed three differential aspects in assessment tool, study sample and MCI diagnosis could cause the somewhat inconsistent conclusions between ours and Lu et al.’s.

Specifically, first, the two studies used slightly different assessment tools. Though it was claimed that the Beijing version of MoCA was used in Lu et al. The items were actually mixed up between the Beijing version and the Changsha version. As noted in their description of the assessment, Lu and colleagues changed at least one item, velvet in the delayed recall task to silk (as in the Changsha version). This modification could improve the diagnostic accuracy due to this culture-specific modification.

Second, the two studies involved different samples. The prevalence of MCI was about 20.0% (1687/8411) in Lu et al.’s study and about 115/1001=11.5% in the current study. Ours is much closer to a pooled MCI prevalence of 12.7% in Chinese population as reported in a recent meta-analysis. This suggests that our sample could be more representative than Lu et al.’s. Third, the MCI diagnostic criteria were different between the two studies. Their diagnosis was mainly based on CDR scores, whereas ours was made upon a more comprehensive and somewhat more strict criteria. It was determined not only based on CDR, but also on GDS supplemented by NPI and HIS, and more importantly on the psychiatrists’ clinical experiences. This diagnosis difference may also be related to the prevalence differences(p.16-17).

And we also deleted such descriptions as “the first large community-based study” throughout the manuscript.

In addition, we added in Discussion section the results from previous smaller studies cited in the Background section in p.5. They both reported similar results as ours that a high sensitivity together with a fair even low specificity with recommended cut-off scores 26. One of them also suggested 21/22 as optimal cutoff as we did (p.16).

2. The description of the how a diagnosis of MCI was reached needs further
elaboration. It is not stated whether the Petersen or other criteria were used, and the specific neuropsychological tests and any cut-offs that might have been used are not listed. This information should be included, since this clinical diagnosis of MCI represents the gold standard against which the MoCA-BJ and MMSE are being judged.

Our Reply:

We elaborated our diagnosis information in p.9.

In our study, the diagnoses of MCI were mainly based on the CDR, GDS, and psychiatrists’ clinical experiences. The detailed elements were as: (1) subjective complaints of memory loss, preferably corroborated by an informant; (2) preservation of general cognitive function; (3) the global CDR score = 0.5; (4) GDS is assessed as level 2 or level 3; (5) intact activities of daily life (ADL); (6) no dementia.

Minor Essential vs. Discretionary Revisions:

3. A relatively low number of participants were diagnosed with dementia (n=21). Since the MoCA is primarily optimized for distinguishing cognitively impaired vs. cognitively intact individuals, perhaps the dementia and MCI groups should be combined for the statistical analyses.

Our Reply:

Thanks for this insightful suggestion. However the reason why we kept the MCI and dementia groups separate is because in this manuscript we also analyzed seven cognitive domains of MoCA in differentiation of MCI/NC and Dem/MCI separately, from which we could discuss the disease progress as from normal aging to MCI, episodic memory was thought to be the earliest and main affected domain, whereas with the disease progression, more basic cognitive functions declined more aggressively than memory (p.12, p.14-15). In addition, the main purpose of this paper is to explore the validation of MoCA-BJ for detection of MCI.

But, anyhow, we do agree that the number of participants in dementia group was small and this could compromise the statistical ability of between-group comparison, therefore we added this as a limitation in the manuscript (p.18).

In addition, following this suggestion, we also analyzed the sensitivity and specificity
of MoCA-BJ for distinguishing cognitively impaired (by combining MCI and dementia together) vs. cognitively intact individuals. As the sensitivity was only increasing a little (72.1%), and the specificity was still below 70% (65.2%), we did not report this analysis results in the revised paper.

4. Given the strong influence of age and in particular, education on MoCA-BJ scores the authors should consider calculating more demographically sensitive cut-points to determine whether adjusted cut-points could improve the utility of the MoCA-BJ in this sample, given that it was slightly better in among participants with >11 years of education.

Our Reply:
Thanks for this helpful suggestion.

We calculated the demographically sensitive cut-off points for 0-6 (10/11), 7-12 (21/22), and 13+ (22/23) educational years, while the optimal sensitivity and specificity were not much more improved when the education was adjusted (0-6: sen. 47.8% & spec. 77.0%; 7-12: sen. 71.4% & spec. 63.6%; 13+: sen. 63.0% & spec. 72.4%).

Also, we further calculated the age-adjusted cut-off points by dividing into 3 age groups: 60-65(23/24), 66-75(20/21), and 76+(13/14) years old. Results did not show much better sensitivity and specificity neither (60-65: sen. 83.3% & spec. 58.0%; 66-75: sen. 67.3% & spec. 71.4%; 76+: sen. 57.6% & spec. 68.0%).

Given there were no significant improvements in terms of screening accuracy, we did not report the above demographically sensitive cut-off points in the revised version.

Reviewing 2

Abstract

1. Although 1056 subjects were recruited, only 1001 subjects were included in all analysis. This point should be clarified in the “Methods” section.

Our Reply:

We clarified that MoCA and MMSE were administered to 1001 Chinese elderly
community dwellers.

2. Linguistic and culture differences are good observations. However, given the sensitivity and specificity provided with either cutoff points (26 or 22), it is not supportive that MoCA-BJ is a suitable screening tool for MCI in the population studied.

Our Reply:

We appreciated and agreed with this comment, and have changed the conclusion from claiming MoCA-BJ being a “suitable” to an “acceptable” screening tool for MCI with a few items needed to be modified throughout the paper.

Background

3. Pages 4-5, Paragraph 1, last sentence, the authors should specify in what population/sample that MoCA demonstrated high sensitivity and specificity for differentiating MCI from normal individuals. “Differentiating” would be more appropriate than “identifying” in this sentence.

Our Reply:

The MoCA has demonstrated high sensitivity and specificity for differentiation MCI from normal individuals in developed countries and areas. We have specified this and added corresponding literatures in p.5.

In addition, “identifying” was replaced by “differentiating” in this sentence as suggested.

4. The literature review regarding MoCA Beijing version validation in China is not adequate. The last sentence in the “Background” section should be revised. A larger scale population-based study entitled “Montreal Cognitive Assessment in Detecting Cognitive Impairment in Chinese Elderly Individuals: A Population- Based Study” by Lu et al has been published in the Journal of Geriatric Psychiatry and Neurology 2011;24:184-190 (PMID: 22228824). The authors should state what additional information this manuscript can contribute.
Our Reply:

We appreciated reviewer pointing this out which was also raised by Reviewer 1.

Basically as our data did not support that MoCA-BJ is a very valid tool for MCI screening, instead we found a couple of items need to be modified to improve the MCI detection ability of MoCA-BJ.

We added this new publication and addressed why further large community-based validation study needed in the Background section (p.6), and discussed three possible reasons for the divergent results between ours and Lu et al.’s(p.16-17). For details please see our response to Reviewer 1’s first question.

Method:

5. Page 7, Paragraph 1: Please state the rationale of recruiting from 3 areas in Beijing and how was the sample size for each area decided.

Our Reply:

The rationale of recruiting from 3 areas in Beijing is that there are huge differences between rural and urban areas, and even between down-town and new town areas, in terms of SES, accessibility to medical facilities, living conditions etc. which could influence their performance on neuropsychological tests (please see p.7).

As to how the sample size for each area was decided, the total number of participants were decided by the funding and resources available, and then the sampling ratio for the three regions was determined by the actual distribution of older adults residing in the three regions in Beijing, which is 57.0%, 20.7%, and 22.3% for New Town, Old Town, and Rural Area respectively (data reported by Beijing Government Council on Aging in 2011, from http://zhengwu.beijing.gov.cn/tjxx/tjgb/P0201111124398948185702.pdf). Eventually we obtained 190 participants from Rural area (17.3%), 238 from Old Town (23.8%), 573 from New Town (57.2%), which roughly met our designed sampling number and ratio.
6. Page 8, Paragraph 1: Please provide the details on “high inter-rater reliability”.

Our Reply:

We added these details in the current version in p.9. We did not start the assessment until all the research assistants and clinicians were intensively trained and high inter-rater reliability (above 90%) was obtained with the support of a consensus diagnosis conference in which the neuropsychological and clinical data were reviewed.

7. Page 8, Paragraph 2: What are the criteria used to diagnose MCI?

Our Reply:

In our study, the diagnoses of MCI were mainly based on the CDR, GDS, and psychiatrists’ clinical experiences. The detailed elements were as: (1) subjective complaints of memory loss, preferably corroborated by an informant; (2) preservation of general cognitive function; (3) the global CDR score = 0.5; (4) GDS is assessed as level 2 or level 3; (5) intact activities of daily life (ADL); (6) no dementia.

8. Page 8, Paragraph 2: Were the psychiatrists blinded of the MoCA and MMSE scores when making clinical diagnoses for all subjects?

Our Reply:

The MoCA-BJ and MMSE were not used to diagnose MCI or dementia (p.9). However, as each participant has one CRF recording all his/her testing information, and the order of administration of the neuropsychological and clinical screening varied among subjects, so the MoCA and MMSE were not totally blinded to psychiatrists.

9. Page 8, Paragraph 3: Please clarify whether pairwise comparisons were performed? If yes, was the significant level adjusted for pairwise post-hoc tests?

Our Reply:

Yes, the pairwise comparisons were performed, and the significant level was adjusted
by Bonferroni method, and this information was added in the revision (p.9-10).

Results:

Table 1:

10. It would be nice to add age- and education-adjusted MoCA and MMSE in the table.

Our Reply:

We added table 3 in which the MoCA and MMSE scores were presented according to Age, Education, and Residence area (p.24).

11. Please clarify the comparisons between any of the two groups: planned contrast tests or pairwise post-hoc tests?

Our Reply:

The pairwise comparisons were performed, and the significant level was adjusted.

Table 2:

12. Please clarify the reasons for different sample size for 3 areas, especially the small sample size in rural area as it will weaken the conclusion drawn for the rural area.

Our Reply:

Please see our Reply to comment No.5 for the reasons for different sample size for 3 areas.

In addition, we included the unequal sample size among areas (small sample size in rural area) as a limitation, as this may compromise the statistical ability of between-group comparisons, and then weaken the conclusion drawn for the rural area.

13. It would be nice to add age- and education-adjusted MoCA and MMSE in the table.
Our Reply:
We added table 3 in which the MoCA and MMSE scores were presented according to Age, Education, and Residence area (p.24).

14. Please clarify the comparisons between any of the two groups: planned contrast tests or pairwise post-hoc tests?

Our Reply:
The pairwise post-hoc tests were performed, and the significant level was adjusted.

Discussion:
15. Page 13, Paragraph 1, the first sentence should be revised as this is not the first population-based study of MoCA in mainland China.

Our Reply:
We have changed this description into “To date, validation studies of the MoCA-BJ in a large community-based Chinese population from both urban and rural areas were rarely reported.” (p.14)

16. Limitations of the current study are not clearly stated.

Our Reply:
We have added several limitations in revised version (p.18). First, the unequal size of among NC, MCI and dementia groups may compromise the statistical ability of between-group comparison. In a similar vein, the small sample size in the rural area may also weaken the conclusion drawn for the rural area. In addition, the study was only conducted in Beijing, however, China is a large country with considerable regional heterogeneity in economy, culture, climate, diet etc. which could affect local residents’ neuropsychological test performance. So sampling stratified from more diverse regions is needed in the future study.

Conclusion:
17. Page 15, Paragraph 2, the first sentence is questionable. Given the sensitivity and specificity provided with either cutoff points (26 or 22), it is not supportive that MoCA-BJ is a suitable screening tool for MCI in the population studied.
Our Reply:
We appreciated and agreed with this comment, and have changed the conclusion from claiming MoCA-BJ being a “suitable” to an “acceptable” screening tool for MCI (with a few items needed to be modified) throughout the paper.

Thank you very much for your time and efforts on our paper. We look forward to hearing from you.

Sincerely yours,
Juan Li