Author’s response to reviews

Title: Role of Gait Speed and Grip Strength in Predicting 10-year Cognitive Decline among Community-dwelling Older People

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Responses to Reviewer #1:

Major comments

[Background]

1. It is difficult to understand a research question of this study. A number of studies demonstrated the association between physical and cognitive function (e.g. Ref. 10-13 and 15-17). In fact, a meta-analysis showed although gait speed is associated with change in fluid cognition, grip strength is not. Additionally, grip strength is strongly associated with MMSE than gait speed (Clouston et al. The Dynamic Relationship Between Physical Function and Cognition in Longitudinal Aging Cohorts, Epidemiol Rev, 2013). What is the question, significance and novelty of this study?
Response: Thanks for reviewer’s comment and we added the prescriptions for our research question, significance and novelty in the background and discussion, such as “Clouston et al., reviewed that gait speed was associated with the change of fluid cognition and handgrip strength was correlated to changes in global cognitive function. Different physical measures might affect different cognitive changes, such as higher-level cognitive change and global cognitive decline.” in line 1-4 of the last paragraph in the background section and “In addition, in the present study, the participants were invited into the study based on a random sample stratified by age and gender and the follow up period was up to 10 years.” in line 3-5 of first paragraph in discussion section.

[Methods]

2. Grouping in gait speed should be conducted by sex. The ratio of participants with slow gait speed was higher in female than in male. Moreover, the percentage of female participants who attend wave 2 only was higher than that of male participants. It is needed to consider the differences.

Response: Thank you for raising this important point. Reviewer #2 also pointed out this issue. Prompted by your and another reviewer’s suggestion, we grouped participants according to gait speed separated by gender and conducted re-analysis. Now this grouping procedure and results are outlined in the main text, tables, and figure. Results were overall robust, and our conclusion was not changed.

3. The baseline MMSE score should be included as a covariate when MMSE is a dependent variable. It is more likely that the baseline score is associated with cognitive decline during follow-up period. DSST is also the same.

Response: Thanks for reviewer’s comment. We explain our models to address your concern. As you see from the 4th paragraph in statistic section, our models have specified covariance between the intercept and slope of cognitive function in the models, which means that the models assumed that the baseline levels of and changes in cognitive function were associated with each other. Therefore, our models have already resolved the issue which you raised as comment #3, and we thus retained the models. Because results of random effects were not our primary interest in this study (please also see from line 11 to line 13in the 4th paragraph in statistic section), we did not add more detailed explanation of random effects in the main text.
[Discussion]

4. The authors explain the reason that slow gait speed and low grip strength are associated with DSST and MMSE, respectively, from second to forth paragraphs in the discussion section. I wonder if these explanations could be argued both ways; that is, current discussions fit both MMSE and DSST (e.g. Reduced gray and white matter volumes in multiple brain regions and white matter hyperintensities may also explain the association between physical dysfunction and global cognitive decline [ref. 58]. Does not that fit DSST?).

Response: Thanks for reviewer’s comment and we had restructured the discussions from the second to forth paragraphs marked in red color. Our results were revised as gait speed was related to DSST decline and handgrip strength was related to MMSE decline in addition to DSST and we restructured the discussions accordingly. Those explanations could be argued both ways but our study showed that global cognitive decline was correlated to poor physical condition by using handgrip strength but not gait speed. We have prescribed those in the 4th paragraph of discussion section.

Minor comments

[Abstract]

5. Please describe the research question of this study in the background section.

Response: Thanks for reviewer’s comment and we had described the research question in line 3-4 of background in abstract section.

[Methods]

6. Are there no exclusion criteria for physical function assessment? Is there no person who is difficult to do physical assessment? (e.g. people cannot walk without a cane).

Response: Thanks for reviewer’s comment. Yes, for those who did not have physical assessment were excluded for analysis. To avoid confusion, we prescribed the sentence as “In addition, participants without assessment for gait speed or handgrip strength were excluded for analysis” in line 6-7 in the 2ndparagraph of study design section. We also prescribed how many participants without physical assessment in the result section for table 1 and 2. However, the reasons why the participants did not have physical assessment were not recorded.
7. The authors pointed out about physical activity [ref.7-9]. Why did not physical activity include as a covariate?

Response: Thank you for pointing out. Reviewer #2 also raised the point. Because our primary research focus was to examine the predictive role of physical function on cognitive decline, we did not take potential mediators into consideration in analysis. Prompted by your comment, we added interpretations regarding indirect effects of physical decline on cognitive impairments. Please see line 4 to line 7 in the 2nd paragraph of discussion section.

[Results]

8. How much is the correlation between MMSE and DSST?

Response: The bivariate correlation was r = .36 regardless of gender. Prompted by your comment, we decided to report the intercorrelations among the key variables (gait speed, handgrip strength, MMSE, and DSST) separated by gender in the 2nd paragraph of results section. Please also see a new appendix for detail.

9. The last sentence in the results section (After including both…). Please provide estimated β and p-values.

Response: Thanks for reviewer’s comment and we reported the estimates and p-values in the main text.

[Discussion]

10. The generalizability of the results of this study should be addressed.

Response: Thanks for reviewer comment and we addressed the generalizability of the results in the line 6-8 in the last paragraph of discussion as “But however, all the participants were recruited by matching age and gender in the community, and therefore the results of the present study could be applied in the community-dwelling older adults without cognitive impairment.”.
Responses to Reviewer 2#:

1. Background

More explanations are needed on why maintaining high levels of physical function may prevent cognitive decline. For example, according to the several physical activity guidelines, engaging in regular physical activity (i.e., do over 150 minutes a week of MVPA; Piercy et al., JAMA, 2018) is favorably associated with cognitive function. Therefore, it is likely that the maintenance of better cognitive function to be influenced by physical activity levels instead of or in addition to physical function levels.

Response: Thanks for reviewer’s comment. Reviewer #1 also raised the point. Because our primary research focus was to examine the predictive role of physical function on cognitive decline, we did not take potential mediators into consideration in analysis. Prompted by your comment, however, we added interpretations regarding indirect effects of physical decline on cognitive impairments. Please see line 4to line 7in the 2nd paragraph of discussion section.

2. Background

This study employed two different cognitive function measures (MMSE and DSST). Did the authors hypothesize that the levels of physical function may differently affect these two cognitive function measures? If yes, this hypothesis needs to be included in the Background section.

Response: Thanks for reviewer’s comment and yes, we hypothesize that the different physical functions may differently affect the two cognitive function measures. We had added the prescription in line 1-4 of the last paragraph of background section.

3. Assessment of physical function

Handgrip strength was divided into five groups according to gender. It is unclear why walking speed measure was not also classified into quintiles by the gender. As Table 1 shows, the gait speed measure appeared to show a gender difference.

Response: Thank you for raising this important point. Reviewer #1 also pointed out this issue. Prompted by your and another reviewer’s suggestion, we grouped participants according to gait speed separated by gender and conducted re-analysis. Now this grouping procedure and results are outlined in the main text, tables, and figure. Results were overall robust, and our conclusion was not changed.
4. Assessment of cognitive function

The MMSE measure was used as a continuous variable. The cut-off points of MMSE (e.g. 23/24) are more common in the gerontology/geriatrics. The reasons for using the continuous MMSE measure need to be included.

Response: As you suggested, we could have operationalized the MMSE measure as a dichotomous variable based on its cut-off point. However, our sample was overall healthy and relatively maintained cognitive function over time: The number of participants who scored below the cut-off of the MMSE was small across waves (n = 17—31). Thus, we decided to use a score of the MMSE as a continuous, not categorical, variable. This is now outlined in the 2nd paragraph of “Assessment of cognitive function (from 2nd to 7th waves)” section in the method.

5. Discussion

It will be useful to see a comparison between physical function results in this sample compared with the general Japanese population. In addition, it should be noted that how many participants had an MMSE score below 24 in this sample.

Response: We have checked average levels of gait speed and handgrip strength in the general populations. However, the sampling and assessment procedures were not described in detail in the published reports of the Annual Physical Fitness Surveys(http://www.mext.go.jp/sports/b_menu/toukei/chousa04/tairyoku/kekka/1368159.htm). Therefore, we were unable to directly compare raw values between our and those existing surveys. Instead, we made clear the generalizability of our results (see from line 6 to line 9 in the 5th paragraph of discussion section).

For the number of participants who scored below the cut-off of the MMSE, we have reported the number at baseline (i.e., 2nd wave) in the last 3 lines of “Assessment of cognitive function (from 2nd to 7th wave)” in Method. Please also see our response #4.