Reviewers report

Title: Oscillometric measure of blood pressure detects association between orthostatic hypotension and depression in population based study of older adults

Version: 1 Date: 3 April 2013

Reviewer: Jess Fiedorowicz

Reviewers report:

Major Compulsory Revisions

1) Without knowing how variables are coded, the presentation of beta-coefficients in the abstract is unclear. Some measure of the magnitude of association should be provided to assess the clinical significance of the findings.

2) The cross-sectional nature of the data limits the ability of the current study to test the “hypoperfusion hypothesis.” Since temporality cannot be accomplished, it is possible that vascular disease contributes to risk for orthostasis and depression though the latter may not be mediated by orthostasis. The clinical assessments, in fact, occurred after, not prior to the assessments of depression. Perhaps, depression or treatments thereof influence risk of orthostasis. The authors acknowledge this in the discussion though the introduction sets up as if testing this hypothesis. Would either acknowledge that this hypothesis cannot be tested with the data or reframe the introduction. I was glad to see the authors plan to reassess this with prospective data and those results will be of great interest.

3) Psychotropic medications, many of which are known to cause orthostatic hypotension, are not included as covariates. This represents an important confound, particularly given the inability of the study design to establish temporality as noted above. While those on antidepressants were not included, those with depression may be more likely to be on other medications (e.g. antipsychotics, alpha-2 antagonists) that could induce hypotension.

4) In Figure 1, it is not clear how the three hypotheses can be teased out based on this figure, particularly, how do the authors demonstrate that depression is due to hypoperfusion as opposed to inflammation or other sequelae of vascular disease? Given this the figure, doesn’t seem to add to the study, which uses a nice sample to establish a relationship between depression and orthostatic hypotension though does not establish temporality or discern any causal relationships. I would suggest deleting this figure and reframing the introduction to discuss testing these hypotheses as more long-term aims than aims of the current study.

5) Table 1 requires some cleaning. Superscript letters appear in somewhat random order. T-tests are used to compare categorical variables across groups, which is not appropriate. It is not clear if assumptions of t-tests were reported. Superscript h is reported twice in the legend. Superscript e reports the same as c
in the legend. Use of fonts in the legend is variable. The sample is large and the standard errors are subsequently small. Standard deviation may communicate variability in the sample more clearly.

6) The sample is reported as a representative sample with weights and clustering. The statistical methods as reported do not appear to appropriately account for weights and clustering. Clustering introduces correlated observations and the method as described would suggest that the cluster was simply included as a covariate in a linear regression model. The statistical methods do not appear to be appropriate though it is possible they simply need to be clarified.

7) Table 2. Methods not clear on how mean change in blood pressure with standing is derived. How many measurements were made and over what time frame?

8) Figure 3, the lines connecting the triangles imply some change over time or across some other continuous measure, but these are distinct groups. Please reformat. Could consider bar graph with standard error bar. Regardless, this graph is probably unnecessary as these differences (at least between OH and no OH) are by definition. Might be easier to just report mean changes per group in the table or within manuscript.

9) Figure 4, as above regarding lines connecting the triangles. Consider alternate presentation. Also, please have y-axis begin at zero or indicate discontinuity so as not to exaggerate apparent differences between groups.

Minor Essential Revisions

1) Abbreviations should be limited and redundant abbreviations eliminated. The opening paragraph uses both LOD and LLD. HIs seems unnecessary. The asymptomatic OH group is alternatively referred to in manuscript as OH and AOH.

2) Some assessments of the sensitivity and specificity of the psychological assessments should be discussed.

3) Please clarify how much time after standing the blood pressure was obtained. Also, how many measurements taken and when (as later reported as mean changes).

4) Results, paragraph 1. It is not as clear from the text description as the figure how the sample of 3144 derived. This figure is very helpful.

5) Results, paragraph 2. Please report N= for number of participants with symptomatic OH in manuscript.

6) Conclusion, paragraph 1. The following statement is not supported by the data: “OH may therefore be a potentially modifiable factor that could be targeted to alleviate depression in the older adults and this strategy may be particularly worthwhile given that the prevalence of OH also increase with age.”

7) Discussion, paragraph 1. References 9% of those with OH are symptomatic. Previously reported as 8.5%. Might prefer 9% for consistency and so as to not over-estimate precision of estimate though will defer to authors.
8) Discussion, paragraph 2. Data supporting the following statement may not apply to transient drops in blood flow that do not correspond to time frame of protein synthesis: “Perfusion deficits do not need to cause ischemia in order to influence brain function since reduced CBF impairs protein synthesis that is crucial for maintaining the integrity of cortical functional maps [10, 35].”

9) Potential for residual confounding should be discussed in limitations.

10) Limitations of the depression measure should similarly be discussed.

11) Figure 2 and the discussion suggests antidepressant use is an exclusion criterion; however this is not listed in the methods. Nor is age between 50 and 60. The rationale for the age restriction is not clear, particularly when the sample is already a sample of older adults.

12) The numbers inside the parentheses in Table 2 are not labeled. They appear to be standard errors.

13) Table 2. It is not clear why statistical tests are only for comparison of OH and SOH. Why is no OH shown? If that is all that is of interest, consider only including these columns.

14) Table 3. If all regression coefficients are unstandardized, please highlight each. Please also replace B with Greek beta. Please specify in legend comparison group (presumably reference group is those without OH though this should be specified in table. Are coefficients for asymptomatic and symptomatic OH modeled concurrently?

15) The authors discuss the possibility of vestibular dizziness as a limitation. Dizziness may also be a feature of anxiety, which is more common in depression, and this can be very briefly mentioned here.

Discretionary Revisions

1) Introduction, paragraphs 3 and 4. These paragraphs provide largely basic information and can likely be condensed some (see also Major Compulsory Revision comment 2).

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.