Reviewer's report

Title: Cardiac ventricular dimensions predict cognitive decline and cerebral blood flow abnormalities in aging men.

Version: 1  Date: 29 November 2012

Reviewer: Andreana Haley

Reviewer's report:

This manuscript reports data from the population study “Men born in 1914.” The authors analyze baseline cardiac ventricular dimensions in relation to baseline and follow-up cognitive test performance as well as follow-up regional cerebral blood flow (rCBF). They conclude that cardiac ventricular dimensions predict cognitive decline and CBF abnormalities in aging men. Considering the importance of cognition for ensuring quality of life in older age, the topic is of interest. However, the statistical analyses need to be revised before we can reasonably assess if the relationships reported by the authors are truly there. I provide some suggestions below, but also recommend a consultation with a biostatistician, as there are multiple issues to be dealt with here including multiple outcomes, repeated measures, covariates, non-random drop out from the longitudinal portion, and lack of baseline measurements for rCBF.

- Major Compulsory Revisions

Abstract:

- Methods paragraph states that “Cognitive performance and CBF were analysed … in subjects …, deceased before 1st follow up and in survivors.” How is this possible if CBF was only measured in survivors per previous sentence?

Introduction:

- The second sentence of the introduction implies that we have much knowledge of the mechanisms which link hypertension to poor cognitive function; yet, the cited paper (Elias et al., 1993) merely examined the correlations between blood pressure and cognition (among many other factors) and did not measure any variables that may serve as mediators or suggested mechanisms. In fact, the authors proceed to offer many more references linking LVH to cognitive dysfunction and cerebral hypoperfusion than they do for hypertension where they claim a greater body of evidence exists. Please revise the statement or offer different references.

- Please introduce FS earlier in the introduction (before the specific study aims) and explain its functional significance for cognition.

- The fact that CBF was available only at follow-up and only on a sub-set of survivors should be made clear in the introduction.

Method:
- Why was HTN defined as HBP>160 mmHg rather than HBP>140 mmHg as in other publications related to the same study (e.g., André-Petersson et al., 2001)?
- Why was education dichotomized rather than used as a continuous variable or classified as in previous publications related to the same study as 0-6, 7-9, 10-13, >13?
- Please provide inter-rater reliability statistics for the two ultrasonographers.
- Some data reduction strategy or multiple comparisons correction is warranted given the number of conducted comparisons (3 cardiac variables x 8 ROIs x 5 cognitive tests).
- Reference 11 is not appropriate for describing the rCBF measurement done by this team.
- The analytic strategy needs to be drastically revised. As stated above, I recommend a consultation with a biostatistician.
1. A t-test comparison of cognitive performance between high LVIDd and normal LVIDd (as described in the Statistics Section) without any adjustments for age, education, other cardiovascular risk variables, and depressive symptoms is inadequate. There are published data out from the same cohort showing cognitive differences related to blood pressure among many other things. The fact that we have multiple outcome variables and repeated testing on some but not all measurements as well as significant non-random drop out also need to be seriously considered and taken into account in the analytic strategy.
3. All rCBF relationships also need to be adjusted for age, blood pressure and other relevant covariates.
4. It may be a good idea to explore non-linear effects, especially where blood pressure and rCBF are concerned.
5. If differences in rCBF are going to be pitched as a potential mechanism driving the poor cognitive function, a mediation model should be tested.
6. The reported statistics need to match what is proposed in the Statistics section. For example, right now, we have tables reporting statistics stratified by hypertension status, but that is not at all described in the Statistics section.

Discussion:
- The discussion needs to be re-written after revisions to the data analyses. Judging by the strength of the reported correlations, I am guessing not all of the discussed relationships will survive…

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests