Reviewer’s report

Title: Pre-diabetes and diabetes are independently associated with adverse cognitive test results: a cross-sectional, population-based study

Version: 0 Date: 12 Oct 2018

Reviewer: Angelo Scuteri

Reviewer’s report:

The research hypothesis is relevant and well formulated. The study population allows testing it.

It seems the statistical approach and the data modeling is somehow redundant and, accordingly, not easy to read. This also impact on the dilution of the potential implications of the main findings.

For instance, it is not clear the added value of having GLM models and multiple regression models as well as so many models, each of group testing different populations because of missing values (PWV), exclusion (stroke cases, diabetes for 2h glucose), adjustment.

Testing a unique study population will simplify presentation and comprehension.

The main point is whether the relationship between alteration in glucose "metabolism" and cognitive function is continuous or is specific for diabetic subjects.

Cognitive tests' scores across groups of "glucose tolerance" do not allow answering the question. What about a post-hoc analysis, to identify which Group differs.

Similarly, having two main set of models - one with glucose as continuous variable and one with multinomial categorical variable (NFG, prediabetes, diabetes) will simplify presentation and comprehension, highlighting the strengths of the study.

Accordingly, the Discussion section also should be shortened and more focused.

Speculations about mechanisms linking glucose to cognition, likely via arterial stiffening/aging, might include - depending on the final results of the proposed models - discussion about:

- glucose-independent (Nutr Metab Cardiovasc Dis. 2008; 18:349-56) and glucose-direct endothelial damage in diabetes (Stroke. 2009; 40: 306-8);

- subclinical inflammation impact on arterial stiffness, independent of metabolic alterations (Atherosclerosis. 2011; 215: 459-64);

- a systemic multiple organs damage "witnessed" by stiffer artery (Int J Cardiol. 2018; 263: 132-137);

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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