Reviewer's report

Title: Brain size and brain/intracranial volume ratio in major mental illness

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Reviewer: Thomas William James Moorhead

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major compulsory revisions

This paper is of interest because it considers the assessment of ICV and TBV. The boundaries of ICV are uncertain in MRI and this measure requires a clear statement of its assessment protocol. The argumentative nature of the abstract held out a promise that the authors would contribute to the methods for assessing TBV and ICV.

Introduction

The introduction starts with an explanation that this report is incidental to an MEG study. The authors consider at length PEG and CT assessments of brain volumes. They note that the MRI literature is extensive and consider for their introduction DeLisi 1999 and McDonald 2004. Further reading reveals that important components of the argument the authors make is based upon recruitment effects in the PEG and CT studies which date back 20 years and more. It is evident that methods and recruitment will have advanced in the past 20 years and this reflection on early work is a limited base upon which to make an argument. I would strongly recommend that the authors rethink and then rewrite the introduction. A quick search of pubmed reveals the following recent publication that looking at tissue volumes in a 1966 cohort.


Methods

It is noted that the MRI scans used in this study were acquired over 13 years. In the methods we are told that the scans to be reported upon were acquired on three different scanners one was a 1.5T GE, one was a 1.5T Philips and one was a 3.0T GE. There is an obvious concern that the use of different scanners may impact on the measures made. This concern needs to be addressed. It may not be a problem but we do need to see evidence of such.

It is also noted in the methods that the measures were all made by the same investigator and that the measures were semi-automated. However, we are not given any indication of repeatability assessments. Testing repeatability in reported measures is standard practice and has been so for many years.

Results

It is stated that there is a significant difference in age between the controls and
the psychosis groups. It is possible that this difference can be adequately accounted for through modelling age as a covariate in a linear model. In this respect and given the broad age range of subjects in the study it would be interesting to see the plots of the measured volumes vs age with group labels, trend-lines would also be helpful. Also I note that Tanskanen et al reports gender separately and in this paper gender is included as a covariate.

Discussion

I was surprised to see tabulated results from other groups in the discussion. Have these groups been consulted about this usage of their data. I found some of the language in the discussion vague. I had expected a more robust defence of the abstract. I do not see in the discussion any indication that the authors have advanced or added to the techniques for assessing ICV and TBV.

**Level of interest:** An article of limited interest

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests