Reviewer’s report

Title: Morphological correlates to cognitive dysfunction in schizophrenia as studied with Bayesian regression

Version: 1 Date: 6 December 2005

Reviewer: Frithjof Kruggel

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There is increasing evidence that schizophrenic patients exhibit morphological differences compared to age-matched controls. The regional characteristics, their origin and their functional correlates remain under debate. This manuscript addresses this debate by studying morphological changes and cognitive abilities in a medium-sized group of psychotic patients vs. controls. Covariates diagnosis, age, gender and volumes of 16 brain substructures were evaluated against 18 neuropsychological subtest scores using pairwise correlation and a Bayesian regression method (reversible jump Markov chain Monte Carlo regression).

The topic of the manuscript is clinically relevant and of interest for the audience of BMC Psychiatry. In most parts, it is easy to follow but contains some errors and leaves some questions open that are detailed below. If these major and minor issues are sufficiently resolved publication may be considered.

Major:
1. The motivation of selecting these 16 anatomical structures is unclear, at least, without referring to previous publications. Assist the reader in understanding why these structures are important.
2. In addition, the motivation of selecting (just) these two statistical tests is unclear.
3. Using pairwise correlation does not disentangle well-known correlation among covariates. Age and gender have a well documented influence on structure volumes - so why not using regression models (perhaps stepwise selected models)? This way, a well-known but, most likely, unsuitable method (correlation) is compared with a less-known but powerful method (Bayesian regression) - and the reader is left with an undecided result (p.13/14).
4. Why were variables age of onset, duration of illness and medication not used as covariates? Here, disease is used as a classificator only. A developmental vs. degenerative (and/or medication-induced) influence might be discriminated.
5. Discuss how much test scores just reflect a disease/medication induced attention deficit. How much depend scores on session time? Was the same temporal sequence of tests used or were they randomized (in both groups)?
6. Is the relatively small sample size an issue when using this Bayesian method?
7. The relatively non-overlap between results of the correlation tests and the Bayesian method requires a more in-depth discussion - at least, from a data-mining perspective. As presented now, there is little discussion about the neurobiological meaning of the results.

Minor:

p.6: 18 covariates and 19 response variable: check again.
p.13: Consider rephrasing "patient material".
p.14: In which way is "medication" introduced in the Bayesian statistic?
p.14: "Pairwise method": This statement is trivial - a different statistic could be used (see issue 3 above).

Table 1: Check the distribution of variables, e.g. specifying SD on ventricle volume is non-informative. The definition of several structural parameters (e.g., corpus callosum, subcortical) in terms of their boundaries is unclear.

Fig.3: Judging from the data points, there is a significant age difference in the patient vs. control group, with the control group not matching the description in the manuscript. Please, revise.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of importance in its field

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

**Statistical review:** Yes

**Declaration of competing interests:**

I declare that I have no competing interests.