Author's response to reviews

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

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Author's response to reviews: see over
Comments to the reviewers regarding the second revised manuscript

“Morphological correlates to cognitive dysfunction in schizophrenia as studied with Bayesian regression” by Lawyer, Nyman, Agartz, Arnborg, Jönsson, Sedvall, Hall

General Comments
Thank you for your reviews of our revised manuscript. We are glad that the changes we made have satisfied the majority of your requests. Professor Friston and Professor Shenton have suggested additional minor clarifications, and we reply to their comments below.

Professor Friston
Thank you again for your helpful suggestions which have indeed improved the presentation of the work. All suggestions have been included for this revision. Some of our changes may require a short explanation.

Comment no. 1
*I would remove the phrase “in a randomly selected subset of the subjects” from the abstract. It would be much clearer and straightforward to describe your cohort, in the abstract and in methods, in terms of the subset you had complete morphological measurements for.*

We have clarified the language in the abstract and the subject description regarding which subjects were included in which part of the study, which, as you point out, should have been more explicit from the beginning.

In addition to the Bayesian decision-theoretic analysis, the paper presents group comparisons of the cognitive tests using the full subject group, and also group comparisons of the morphological measures using all subjects for which each individual measure was available. These are previously unpublished results, which makes it difficult to remove these subjects from the study.

Comment no. 6
*You report the intra-class correlation coefficient for the intracranial volume and other measures. Given that these measures, with the exception of the hand drawn regions of interest, were defined using an automated procedure, why was the correlation coefficient less than 1? I think you have to describe at what point you lose the 100% reliability when using the automated protocols.*

More detail has been added to the methods section, which we hope makes clear that all of the measures relied to some degree on operator input.

Comment no. 12
*Could you provide corrected p-values in your tables as well as the uncorrected p-values?*
We have now applied Benjamini’s False Discovery Rate to suggest an appropriate level of significance, which is now stated in the table legend. We have also added a few words introducing this concept in the methods section.

**Professor Kruggel**

Thank you for your review. We are glad that the manuscript now meets your approval.

**Professor Shenton**

Thank you for once again reviewing our work, and spotting a remaining weakness.

_The only remaining comment I have is how they addressed possible gender issues, which I listed as a concern, but which has not been addressed._

The issue of gender is important, which is why gender was included as a covariate in our statistical model. This was presented in the methods section of our revised manuscript. It has now also been stated in the subject description as we want to explicitly mention that possible effects of gender have been addressed in the statistical model. Thank you for suggesting an improvement here.