Reviewer's report

Title: Distribution of tract deficits in schizophrenia

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Reviewer: Julia Friederike Sowislo

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This manuscript reports the results of a magnetic resonance imaging study in 21 patients with schizophrenia and 21 controls. Converging with previous literature, the study found white matter diffusion deficient in medial frontal regions.

In general I enjoyed reading the paper: As neurodegenerative aspects of schizophrenia are still a matter of dispute, studies in this area are crucial to contemporary psychiatric research. Methodologically, the study seems to be sound and the data analysis to be solid. By using three different approaches to analyze the diffusion tensor images (DTI) the authors increased the reliability of their findings.

I do mainly have concerns with regards to the following aspects:

First, I ask the authors to elaborate more on the novelty of the findings (in contrast to the novelty of the method). Second, it seems to me that the article addresses a rather specialized audience. As can been seen from my below comments, I would suggest that the author clarify some issues in order to make the article readable for a wider audience. I think that clarifications would strengthen the contribution of the current research.

- Minor Essential Revisions

(1) I would like the authors to precisely indicate what can be learnt from this article over and above what is known from previous meta-analysis of DTI in schizophrenia (e.g., Ellsion-Wright & Bullmore, 2009; Kanaan et al., 2005).

(2) The authors claim that one major purpose of the article was to relate white matter tract differences in schizophrenia to changes in gray matter (p.5). However, as far as I understood, the study did not detect any gray matter changes in schizophrenics as compared to controls. Can the authors discuss what the null-finding in gray matter changes means with regard to the initial research purpose?

(3) Relatedly, as the study could not replicate the previously found volumetric changes in gray and white matter, I wonder whether the study might be underpowered. The authors discussed the drop-out of seven subjects and the possibility of type 2 error. Is there any evidence for the drop-out being selective? Could the authors give justification for the chosen sample size (i.e., show the results of a power analysis)?
White matter changes were found using diffusion analyses but not using volumetry. Can the authors give some examples for less familiar readers demonstrating why changes in fractional anisotropy do not necessarily have to result in volumetric changes?

In addition to the 21 patients who met diagnosis of schizophrenia, the authors included two patients who met diagnosis of schizoaffective disorder. I would question the authors to explain why they included these two schizoaffective patients.

The authors state that the control participants were matched (p.3). They report that there were no significant differences in variables that are supposed to affect fractional anisotropy such as age (e.g., Pefferbaum et al., 2000), IQ (e.g., Schmithorst et al., 2005), gender, and handedness (e.g., Westerhausen et al., 2003). However, the groups do not seem to be matched with regard to these variables (e.g., 17 males in the study group vs. 14 males in the study group). Can the authors indicate how the matching was done?

The authors write that “either independent sample t-test or Mann Whitney U was employed to compare age between groups” (p.14). If I understood correctly, they tested for age differences between the two study groups. I would like the authors to indicate which of both tests they employed.

The authors argue that some structural changes in schizophrenia may not represent a primary pathology, but result from the symptoms. To shed more light on these issues the authors suggest conducting studies that examine potential confounders. I would ask the authors to give some examples of confounding variables. Would it be possible to add some additional analyses to the study which include some of these variables?

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

Quality of written English: Acceptable

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.