Reviewer's report

Title: Distribution of tract deficits in schizophrenia

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Reviewer: Richard Antony Alexander Kanaan

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This is a small volumetric and diffusion study of schizophrenic patients vs controls. They find no volumetric but widespread diffusion differences in the patient group. Though it sets the scene ambitiously with its triple analyses, it's not clear that the methods are combined in any complementary manner and the sample is almost certainly too small for appropriate power.

Major Compulsory Revisions
1. Methods – a power analysis is clearly missing. It’s not essential that the study is properly powered (it probably isn’t) but the results are very hard to interpret without it.
2. Methods – were the volumetric scans that were excluded for motion artefact still employed for the tractography definition process? How can this be justified?
3. Results – there appears to be a huge multiple comparisons problem with the regional analysis, and I suspect any reasonable approach to correcting this would eliminate all results.
4. Results – was the tract data normally distributed – the authors mention testing this, but don’t give the results – to justify using an ANCOVA?

Discretionary Revisions
5. Background – this is under-referenced. The authors should acknowledge the wide range of tracts implicated in previous studies – not just the ones they are interested in.
6. Background – why discuss spatial progression when this study does not appear relevant to its investigation?
7. Background – was there ever an intention to combine the 3 methods? It’s not clear how these were meant to complement each other. Why use the tractography at all, when the regional method you have gives meaningful localisation?
8. Methods – why include subjects with schizoaffective disorder? Though the effects of two subjects may be small, they should really consider some kind of sensitivity analysis.
9. Methods – the statement that additional medications were an exclusion unless the investigator didn’t think so seems completely meaningless to me. Either clarify, or drop it.
10. Methods – I don’t understand the nature of the tractography process used,
and its talk of ‘gates’. The authors should provide some broad outline of how the software worked for those unfamiliar with the method.

11. Methods – an intra-rater reliability is mentioned – what was this defined on (which tractography measure)?

12. Methods - Why was FDR used for the VBM analysis, and not SPM’s more usual FWE?

13. Methods – it is unclear exactly which data was taken from the TBSS through to the regional analysis.

14. Methods – why was age used as a covariate for the VBA but not for its regional comparison?

**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