Reviewer's report

Title: Obsessive-compulsive disorder is a heterogeneous disorder: Evidence from diffusion tensor imaging and magnetization transfer imaging

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Reviewer: Kathrin Koch

Reviewer's report:

Glahn and colleagues investigated structural brain abnormalities in 14 male and unmedicated patients with OCD compared to healthy controls. They used DTI to investigate potential alterations in fractional anisotropy (FA) and apparent diffusion coefficients (ADC) and the method of magnetization transfer imaging (MTI). They report altered integrity of tissue structure in patients compared to healthy controls in various regions. Furthermore, they find Y-BOCS scores for compulsions to correlate negatively with ADC-maps in the left nucleus lentiformis and the cingulum. Glahn and colleagues conclude from their findings that OCD is a heterogeneous disorder with distinct neural correlates across symptom dimensions.

Due to the methods used (i.e., combination of DTI and MTI) the study is interesting and innovative. However, there are several aspects that should be taken into consideration before the study can be recommended for publication:

- In the introduction previous findings regarding white matter changes in OCD are reported. Here, the authors may want to add a recent review by Koch et al. (2014, J Psychiatr Res) on DTI studies in OCD and take into consideration its main conclusion which indicates that the cingulate bundle, the corpus callosum and the anterior limb of the internal capsule seem to be most commonly affected by decreased white matter integrity in adult OCD patients.

- The introduction addresses the fact that patients diagnosed with OCD widely vary according to symptom type, different kinds of obsessions and compulsions, severity, age of onset and comorbidities. Here, medication should be added as another relevant influencing factor that varies between patients.

- Reasons why the method of MTI was applied in addition to DTI are explained in the introduction, however only very shortly. The manuscript would certainly profit from a more extensive explanation of the advantages of MTI and the possibilities it offers in comparison to the method of DTI.

- Methods: Please provide more information on how FA and ADC maps were calculated (i.e., with a toolbox, inhouse batches..).

- Methods: It is stated that after calculating the FA and ADC maps, images were preprocessed and analyzed by SPM2 using an approach adopted from VBM. Some more details on data preprocessing should be provided, such as which approach has been used? Was this a toolbox? Has DARTEL been used for normalization?
- Methods: In the “statistical analysis” section it is written that group comparison of OCD patients and healthy controls was performed in SPM2 using the model 'compare populations: one scan/subject (ANCOVA)'. This description is difficult to understand for people unfamiliar with the SPM2 interface. If an ANCOVA has been performed, this should simply be stated including the definition of the factors (e.g., factor GROUP) and the covariate(s) which are not specified in the methods section.

- Results: The results reported in the results section do partly not correspond to the results reported in the tables (e.g., regarding decreased FA in patients, in the text of the results section the striatum is mentioned which is, however, not mentioned in the table). Moreover, the results reported in the results section do partly not correspond to the results reported in the abstract (e.g., regarding MTR increased in patients, in the text of the results section frontal areas are reported, while the abstract mentions parietal areas).

- Figures: The figures display structural alterations on a threshold of p<0.01 uncorrected (with different spatial extent thresholds). Normally, the display of the results should correspond to the threshold that has been applied in the analyses.

- Discussion: Regarding the MTR alterations in patients the authors refer to previous studies showing that MTR reductions correlate with myelin and axonal loss in the white matter in post mortem tissue. In the present study, however, patients showed an increase in MTR in several regions. What does this indicate then? This should be discussed. Moreover, the negative correlation between ADC values and YBOCS compulsion scores is a bit contraintuitive at first sight as one would normally expect higher clinical scores to be related to a decrease in structural integrity (i.e., an increase in ADC values which would mean a positive correlation). This finding should be discussed a bit more in detail, for instance one could assume that increased structure may favor hypertonic state which has been shown to be associated with compulsive behavior. This is, of course, speculative, but the discussion would probably profit from a bit more detailed discussion of this aspect.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests