Reviewer's report

Title: Diffusion Tensor Imaging in Neuropsychiatric Systemic Lupus Erythematosus

Version: 1 Date: 14 December 2009

Reviewer: Kathrin Koch

Reviewer's report:

This is an interesting paper which employs novel methods to investigate white matter alterations in NPSLE and SLE. It is well-written, findings are related to current status of research and potential mechanisms underlying these alterations are discussed. There are some aspects that should be taken into consideration before the manuscript can be recommended for publication:

- Major compulsory revisions:

  - The authors report mean diffusivity and discuss this finding with regard to potential neuropathological mechanisms. A more specific analysis of the directionality of this increased diffusivity in NPSLE (i.e. regarding potential alterations in radial and axial diffusivity) would provide additional information on the mechanisms underlying these alterations (i.e. increased axial diffusion is often interpreted in light of axonal alterations whereas increased radial diffusion is assumed to indicate decreased myelination). The authors might want to perform these additional analyses which can be easily done with TBSS.

  - As indicated in Tab. 2 multiple white matter alterations were detectable in the high resolution scans in the SLE group. At first sight, this is surprising given no differences between SLE and controls in the TBSS analyses. This might have methodological reasons which, however, should at least be addressed in the discussion.

  - No information on duration of illness or number of NPSLE episodes is given. In light of the fact that old infarcts were obviously not decisive regarding the white matter alterations detected in the NPSLE patient group it would be interesting to know if duration of illness had an influence of the results (with e.g. a longer duration of illness in the NPSLE group which might have been associated with stronger (accumulative) degenerative processes across time).

  - The diagnostic differentiation between SLE and NPSLE is known to be quite difficult in some cases. The authors declare the presence of acute stroke or transient ischemic attack (TIA), acute confusional state, moderate cognitive dysfunction, seizures, or psychosis as diagnostic criteria for NPSLE. However, no information on the screenings and methods used to determine the existence of these criteria are provided (e.g. how have potential cognitive dysfunctions been assessed, which screening procedure has been applied to determine presence of psychosis etc.). And, maybe even more important, have other potential causes for manifestation of neuropsychiatric symptoms (like e.g.
infection or medication side-effects) been excluded? More information regarding diagnosis of NPSLE should be given.

- Minor essential revisions:

- The threshold used for the mean FA skeleton should be provided as results are influenced by this threshold (as the authors probably know a default of FA>0.2 is recommended which can be adapted, however).

- The technique of DTI is explained on p. 3 (first page of the introduction). Therefore, the explanation on p. 4 “(...) a technique that yields quantitative measures and directionality of water mobility [15]” is redundant and should be removed.

- Finally, the authors might want to stress the timeliness of their method by mentioning that TBSS is increasingly being used for investigation of white matter alterations in various diseases like schizophrenia (here, the authors might want to refer to a recent study by Koch et al., Eur Arch Psychiatry Clin Neurosci.) or depression (here, the authors might want to refer to a recent study by Kieseppä T et al., J. Affect Disord).

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

**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