Author's response to reviews

Title: Cerebrospinal fluid CXCL13 in Lyme neuroborreliosis and asymptomatic HIV infection

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Author's response to reviews: see over
Cover Letter

Revised version of “Cerebrospinal fluid CXCL13 in Lyme neuroborreliosis and asymptomatic HIV infection”

The authors are most thankful for the reviewers’ work and are of the opinion that the revision has significantly improved the article. Here follows a point-by-point description of changes made in response to the concerns raised by the reviewers.

General changes
- Table 1 has been expanded to include data on clinical symptoms for the LNB patients.

Reviewer 1: Tobias Rupprecht
- A reference to the study by van Burgel et al. is now included in the Introduction section.
- Sections on how many of the LNB patients that had a positive AI is now included in the Results section. 16 of 19 LNB patients in the cross-sectional study and 23 of 25 patients in the longitudinal study had a positive AI. As these patients constitute an absolute majority of the patients, no separate calculation of their respective CXCL13 levels have been made.
- The fact that the median value of CXCL13 in the LNB patients in the cross-sectional study is lower than in previous studies has now been highlighted. In the ROC analysis that gave the suggested cut-off value of 44 pg/mL data from both the cross-sectional and the longitudinal study was included.
- The conclusion on the diagnostic potential of CSF CXCL13 in LNB has been attenuated in the Conclusion section and in the Abstract.

Reviewer 2: Kenneth Tyler
- Sections on the longitudinal study have been move forward accentuating their importance.
- Data on the correlation between CSF mononuclear cell count and CXCL13 has been included in the text and in added figures. Data on the concentration of specific types of mononuclear leukocytes in the CSF was not available for this study.
- References to other infectious diseases in which elevated CSF CXCL13 concentrations have been reported has been added and the novelty factor of the findings has been downplayed.
- Markers for median and interquartile range have been added to Figure 3 (formerly Figure 1) showing CSF CXCL13 levels in HIV, LNB and controls. Figures showing the correlation between CSF mononuclear cells and CXCL13 in HIV and LNB have been added (Figure 4). The data on the quotients of mononuclear cells and CXCL13 on which Figure 2 (formerly Figure 3) is based show a non-Gaussian distribution and the correlation analysis is made
using the non-parametric Spearman rank order correlation why the addition of a best-fit line is not appropriate.

- What extra information is added by the analysis of CSF CXCL13 over what is already known from the analysis of CSF mononuclear cells is covered in the third paragraph of the Discussion and has also been expanded in the last paragraph of the Discussion.

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Sincerely,

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