Author's response to reviews

Title: Pros and cons of a prion-like pathogenesis in Parkinson's disease

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Author's response to reviews:

Dear Sir,

Please find attached our revised manuscript “Pros and cons of a prion-like pathogenesis in Parkinson’s disease” for possible publication as a debate in BMC Neurology.

We are grateful for the very helpful comments of the reviewers. Our revision covers all of their suggestions and remarks (changes in the manuscript were highlighted by bold letters). In detail, we wish to respond as follows:

Reviewer: Zeev Meiner

point 1: More details on prion disorders were included in the background section of the abstract (page 2, 2nd paragraph). As suggested, we also added the finding of alpha-synuclein aggregates in dopaminergic brain transplants of PD patients to the discussion paragraph (page 2). The summary was shortened, and the main message of the paper was drafted more precisely.

point 2: We added the study by Selikhova et al. published in Brain 2009 (reference no. 2) for more detailed information on the frequency of Alzheimer type histopathology in PD patients (page 4, lines 4-7).

The adequate reference for the sentence “Misfolded SNCA is also able to spread over adjacent neurons and to induce degenerative changes in transfected cells” was added (reference no. 4) (page 4, line 15).

As suggested, two post-mortem studies showing alpha-synuclein positive Lewy bodies in embryonic dopamine cells of beforehand transplanted PD patients were mentioned in the background section (page 4, lines 15-18).

point 3: We thank the reviewer for his important remarks concerning the improvement of our discussion section. As suggested, we divided the second paragraph into a new section on “Molecular biology of alpha-synuclein” (page 6, 1st paragraph) and into the former heading “Arguments for a prion-like pathogenesis in PD” (page 6, 2nd paragraph). The latter was broadened by the suggested aspects of genetic overlap between prion diseases and PD (page 7, last paragraph).

In the last paragraph, we added the important consideration of the exclusively
infectious character of prion diseases after iatrogenic procedures (page 10, 1st paragraph).

Finally, we corrected the typing error on page 5, line 20.

We resubmit the revised manuscript and hope that these modifications and comments will be sufficient to permit the acceptance of our paper for publication. We thank you again for the consideration of this manuscript.

Sincerely yours,

Ruediger Hilker, MD