Reviewer’s report

Title: Pyramidal system involvement in progressive supranuclear palsy - a clinico-pathological correlation

Version: 2 Date: 28 Aug 2018

Reviewer: Gesine Respondek

Reviewer’s report:

In their study "Pyramidal system involvement in progressive supranuclear palsy - a clinico-pathological correlation", Zuzana Stejskalova and colleagues analysed AT-8 tau pathology in the pyramidal system and retrospective clinical data in 25 autopsy-confirmed patients with PSP with different clinical presentations. They found more tau pathology in the pyramidal system in PSP patients with Richardson's Syndrome. The severity of clinical features associated with the pyramidal system did not correlate with the severity of pyramidal tract pathology and did not differ across different PSP phenotypes.

Involvement of the pyramidal system in PSP has been reported earlier. A novel aspect of this study is the comparison of different PSP phenotypes. While this is important, I have several concerns regarding methodology and interpretations of results in this paper:

Case selection:

* It needs to be clarified how many patients contributed to the clinical and pathological findings. In my understanding, only 19 patients are included into final analysis. In that case, it is redundant to talk about 25 patients or it needs to be clarified what kind of additional information is taken out of these 6 excluded cases.

Clinical data:

* How detailed was the retrospective clinical data and at what stage of the disease was it collected? It is conceivable that clinical information was not available shortly before death in many cases, which could explain the lack of correlation between pathological findings. This should be discussed.

* The presented new semiquantitative scoring system requires fairly detailed clinical data. Was it really possible to retrospectively extract spastic dysarthria versus bulbar dysarthria, spasticity versus rigor, decreased gag reflex and soft palate palsy?

* Authors should discuss that the lack of validation of their scoring system (and lack of detailed clinical data?) might contribute to the failure to find any correlation between pathological and clinical pyramidal tract impairment.
Pathological data:

* Pathological findings on neuronal loss in the pyramidal tract regions in this cohort should be displayed in results and discussed.

Statistics:

* Besides the mean and median of RS and non-RS of total neuropathological scores, SD or range should be given.

* Multiple comparison correction should be applied.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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