Reviewer’s report

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

Version: 2 Date: 03 Sep 2018

Reviewer: Kevin Bieniek

Reviewer’s report:

"Pyramidal system involvement in progressive supranuclear palsy - a clinico-pathological correlation" by Stejskalova et al. is a descriptive study regarding the presence of motor system pathology and pyramidal signs in autopsy-confirmed PSP cases with different clinical subtypes. The authors employ semi-quantitative scoring systems to assess bulbar signs, pseudobulbar signs, and spasticity as well as tau-immunoreactive neurofibrillary tangles, coiled bodies, tufted astrocytes, and neuropil threads in various neuroanatomical regions. The cohort is well characterized (predominantly in the Supplemental Material) and the manuscript is well-written. My biggest concern is that while a statistical significance was detected between total neuropathological score in motor regions of PSP-Richardson versus PSP-non-Richardson cases, this finding does not appear to translate to a meaningful finding of clinical or pathological relevance. Specifically, the authors state "there were no statistically significant differences in any individual domain between PSP-RS and non-RS patients" (pathology) and "we found no significant difference between the RS and non-RS subgroups relative to their clinical scores and their sum". Greater clarity is needed regarding what the "individual domain" represents - does the total score summate all types of tau immunoreactive pathologies (NFTs, TAs, CBs)? Are there differences in total scores of specific pathological lesions? Does a domain represent all pathologies in a single anatomical regions? Some additional comments regarding the manuscript are as follows:

A) Sections 2.5 (Statistical methods) and 3 (Results) appear to contradict each other. Section 2.5 states neuropathological data were available for all 25 study cases and clinical data was "incomplete in 3 cases and these patients were eliminated from the statistical analysis" (together suggesting a total of 3 cases excluded). The beginning of Section 3 states "six patients were excluded from statistical analysis because of incomplete clinical or neuropathological data".

B) Table 2 is quite difficult to read. The table would benefit from either inverting the table to a horizontal format or using alternate shading of consecutive rows to delineate the different semi-quantitative scores.

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

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

Yes

Are the conclusions drawn adequately supported by the data shown?
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