Reviewer's report

Title: Proteinase-activated receptor 2 and disease biomarkers in cerebrospinal fluid in cases with autopsy-confirmed prion diseases and other neurodegenerative diseases.

Version: 2 Date: 29 December 2014

Reviewer: Alberto Benussi

Reviewer's report:

Comments to the Author

Rohan and colleagues tried to investigate the clinical utility of CSF PAR-2 levels in patients with prion disease considering that PAR-2 knockout scrapie-inoculated mice showed delayed onset of symptoms and longer survival than PAR-2 wild-type mice. This study is interesting and, although authors do not find differences in CSF levels of PAR-2 between prion disease and neurodegenerative disorders, it enriches the knowledge of biomarkers in the aspect of dementia in which disease specific biomarkers are currently lacking. In addition, all cases were pathologically examined. However there are several minor revision to be made.

Comments

Abstract:

- The second sentence of the background section (line 32-34) is not very clear (cerebrospinal fluid is not a marker of neuronal damage, maybe cerebrospinal fluid tau is) and should be reviewed for english (eg. neurodegenerations could be changed in neurodegenerative disorders).

- In the objective section of the abstract (line 35) the acronym CSF should be reported at the first citation (line 33) and not at line 35.

- Please use the same terms across the manuscript (phospho-tau at line 36 and phospho tau at line 39, as well as total-tau and total tau). Review punctuation and the use of “and”.

- Review syntax and english at line 44-46.

- Review english at line 49 (high total-tau CSF levels protein positivity). Correctly identify the acronym CJD in this line.

Main text:

- At line 61 the authors could clarify the mechanisms underlying PAR activation (eg. activated by proteolytic cleavage of the extracellular amino terminus).
- When identifying acronyms or abbreviations the authors should keep the same term throughout the whole text (eg. P-tau181p at line 72 and then p-tau at line 78; this goes also with A#(1–42) and A#.

- Review line 84 for english: (eg. were assessed clinically and neuropsychologically, underwent....)

- Line 89: “see Table 2”: are the authors referring to the table in the supplementary material? There is no Table 2 in the manuscript, please clarify.

Table 1: third row, fourth column: “2-84” this is a range, not the median, please correct.

Line 111: correct abbreviations “B-amy”, etc.)

When reporting p-values, perhaps it is best to write only 3 digits after the comma (e.g.. p=0.005, or p<0.001 for cases with very low p-value and do not use exponentials)

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests