Reviewer’s report

Title: Diagnostic accuracy of cerebrospinal fluid protein markers for sporadic Creutzfeldt-Jakob disease in Canada: a 6-year prospective study

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Reviewer: Michael Andreas A Tranulis

Reviewer’s report:

This contribution by Coulthart and co-workers examines the diagnostic usefulness of spinal fluid proteins (14-3-3, tau & S-100B) for sporadic CJD. This is an area of considerable interest and with some variations between reports from different labs.

This is a well-composed and well-presented contribution that will be of interest in this field. The authors particularly advocate the use of likelihood ratios (LRs), which is elaborated on in the discussion, which is almost exclusively dedicated to statistical analysis/discussion.

This is certainly important and of great interest for the reader, therefore, the editors might find it useful to have a separate expert review of this part of the study. To this reader, which is not a bio-mathematical expert, the statistics and presentation and discussion of the data seem correct, balanced and reasonable. Figures and tables are easy to interpret and the use of confidence intervals is highly welcome.

The authors are advised to use the term non-CJD (as they do in the abstract and fig 1) and not nCJD, which might cause unnecessary confusion, being similar to sCJD, vCJD, gCJD etc., which are abbreviations for sub-groups of CJD.

It is well documented that the proteins in question, 14-3-3, tau and S-100B are pretty robust and stable, allowing reliable measurements even after prolonged sub-optimal storage. Nevertheless, this reader finds the materials and methods part dealing with sample storage (temperature, duration etc.), preparation/extraction, any F/T cycles, master standards for calibration (fresh?, storage?, how and for long?, stored diluted?), to be an area the authors might have a look at. Correct treatment of samples and reagents is of pivotal importance to insure data integrity – errs in this department cannot be corrected by statistical analysis. For example, in this study 14-3-3 is analyzed first and then, based upon sample availability and the outcome of the 14-3-3 analysis, S-100B and tau are analyzed – how was the sample stored during this time? Frozen or at 4° C? Some readers, including this one, would find this information to be interesting and something that would contribute to the completeness and quality of this paper.

References 3 and 26 are incomplete.

This reader evaluates the current manuscript as a valuable and scientifically sound contribution that meets all standard criteria for such reports and therefore
favors its publication.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I have no competing interests.