Author’s response to reviews

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

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Author’s response to reviews: see over
Dear Mr. Bongcayao,

We are again grateful for the Journal’s prompt and thorough review of our manuscript, and for the insightful criticisms provided by the reviewers.

A second revision of the manuscript has now been submitted to the Journal, taking into account Reviewer #2’s single additional suggestion in response to the first revision. As before, to facilitate review of our proposed revisions, we have reproduced the reviewer’s original comment in its entirety below with our response and supporting discussion immediately below in a contrasting font. Where page and line numbers are cited, they refer to the revised version of the MS.

We apologize for the fact that, as Reviewer #2 notes, in the process of PDF formatting during upload of the first revision not all of the changes (and apparently none of the MS Word comments) were clearly reproduced. To address this, we have indicated the single deleted section in the current revision with strikethrough, and the inserted section with which we replaced it in blue. In addition, as we interpreted the response to our first revised version to indicate that our previously suggested changes were acceptable, for ease of final review we have incorporated all of those changes into the current version.

Again, if the Editor and/or reviewer disagree in any way with our proposed response, we would be more than happy to clarify further or to reconsider.

Very best regards,

Michael B. Coulthart, PhD
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Overall, the authors seem to have responded appropriately to the queries raised in my review. However, I could not easily locate the additions and/or deletions to the text for Comments 5b and 5c at the pages and lines indicated. Both comments essentially deal with how cases are classified and analyzed. In response to these comments, the authors apparently have added a lengthy explanation as of why “probable” sCJD and non-sCJD cases could be handled differently and the criteria for classifying cases as sCJD or fCJD. I would recommend that case populations be clearly but succinctly (if possible) defined in the Methods or Results section.

Response: We thank the reviewer for his favorable overall response to our first round of revisions, and once again for his insightful original comments on our case-classification criteria. We also agree with his current suggestion that we could be more concise in our exposition in this area. More specifically, we realized that for purposes of discussion we need only provide an estimate of prevalence of gCJD in our CSF-testing population (and not also in general surveillance populations), and a literature reference to support our understanding that the diagnostic accuracies of CSF 14-3-3, tau and S100B proteins for gCJD are similar to those for sCJD. In light of these considerations, we therefore replaced a 592-word section of the text (Discussion p 22 line 17 – p 24 line 16, strikethrough format) with a more concise 301-word version (Discussion p 24 line 18 – p 25 line 15, blue color). Although we take note of the reviewer’s suggestion that this material could be relocated to Methods or Results, we also feel that the criteria used to define case populations are already well defined in Methods and Results, and we respectfully suggest that for continuity of presentation a discursive response to his original comments 5b and 5c is appropriately placed in the Discussion along with consideration of other potential limitations of the study.