Reviewer's report

Title: Impact of the clinical context on the 14-3-3 test, based on the analysis of a Spanish cohort of suspected sporadic CJD patients

Version: 1 Date: 28 April 2006

Reviewer: Inga Zerr

Reviewer's report:

The authors investigate in their study a population of 672 suspected CJD patients in Spain for the relevance of the 14-3-3 test for sufficient clinical diagnosis. Earlier studies on sensitivity and specificity were performed on predefined patients who might not represent clinical practice. Therefore the authors investigated a population of which samples for 14-3-3 testing were sent to the reference centre as these patients have clinical suspicion of CJD. Before testing, an initial classification according to the WHO criteria into probable (n=115), possible (n=73) and other (n=484) was done. Completed by follow-up information and, if available, autopsy a final classification was established as definite (n=75), probable (n=102) and non-CJD (n=495) (possible excluded). 14-3-3 had a high efficiency of 94.5%. There was no difference between the CJD patients with positive or negative 14-3-3 regarding age at onset, survival time, and date of LP within disease course. Faint bands in Western Blot were interpreted as negative: this resulted in a slightly lower sensitivity and higher specificity than in the literature described.

14-3-3 was able to moderately increase diagnostic accuracy compared to the clinical symptoms alone. Beside this, 14-3-3 is most useful in supporting the clinical diagnosis, but has to be handled with care when it is not in agreement with clinical suspicion. This study focuses on the very interesting point of the relevance of the 14-3-3 test in suspected CJD patients. Beside high values for sensitivity and specificity in the literature, there are also studies on false positive test results in varying diseases. The authors support in this study the idea of a high impact of 14-3-3 when used in clinically suspected patients and not for screening without clinical data. The high patient number and the long follow-up lead to fine and consistent data.

For improving the article we suggest some minor revisions:

1. The title should be shortened and more focussed
2. Similar data on a substantially smaller number of patients (n=36) were recently published by Blennow in 2005. This study should be cited and discussed.
3. On page 8, citation number 13, the name of the author should be corrected in â€œGeschwindâ€ (as in the references).
4. It would be interesting, what kind of CJD patients had a false negative result (n=22): what codon 129 polymorphism, PrPsc isoform, further CSF parameters such as tau, additional data on MRI and EEG for this special group?

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

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

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests