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Letters to the Editor

Free and Cued Selective Reminding Test sensitivity

We read with great interest the recent article by Teichmann et al. [1], who presented results of the Free and Cued Selective Reminding Test (FCSRT) accuracy to differentiate typical (amnestic) Alzheimer's disease (AD) from other neurodegenerative diseases. The authors assessed FCSRT in a group of 992 individuals, most of them with the diagnosis of AD, and stated that FCSRT would have a sensitivity of 100% and a specificity of 75% to diagnose typical AD. A diagnostic test for amnestic variant of AD that is very sensitive and specific in early stages of dementia would be extremely useful to distinguish it more accurately from other neurodegenerative diseases, especially in the context of possible disease-modifying therapy, probably effective in early or prodromic phases. FCSRT has been suggested by the International Working Group as a test to characterize amnestic syndrome of hippocampal type [2] and in fact has been demonstrating high correlation with AD pathology [3] and high sensitivity to predict mild cognitive impairment conversion to dementia [4].

However, we consider that the methods used to analyze the test performance introduced some bias to the results. The authors stated, in the methods section, that FCSRT was used to select patients to enter the study, rather than other test or set of tests, that would diagnose a patient as having amnestic variant of AD; that is, all patients with amnestic hippocampal syndrome were selected by the same instrument that is in fact being tested. Indeed, the sensitivity described in table 1 was 100%, both for AD dementia as for prodromal AD. The use of biomarkers for AD does not help in the mitigation of this bias, as this simply implies that patients included in the study had most likely AD pathology.

Both the sensitivity and specificity of a test must be established regardless of the means for which the true diagnosis was established. In other words, the diagnostic test being evaluated should not be a part of the information used to establish the diagnosis [5]. Because there is no gold standard test for the presence of hippocampal amnestic deficits, it would be more useful to compare FCSRT with a larger battery of tests that could more accurately determine the presence of hippocampal amnestic deficits earlier in the disease course. One of the problems arising from this biased analysis is that it does not identify individuals above the cut-off point in the FCSRT and that do not have beta amyloid positive biomarkers. Another problem in establishing *a priori* sensitivity in 100% is the implicit suggestion that the diagnosis of an amnestic syndrome of hippocampal type could be excluded in an individual with a FCSRT score above the cut-off point. Both conclusions cannot be drawn from the results of this study.

In conclusion, although FCSRT may be useful in determining amnestic syndromes, it is not possible to conclude from this study that the sensitivity of the scale is 100%, because some patients with amnestic presentation of AD may go undetected by this test.

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