

Impact of the 2017 revisions to McDonald criteria on the diagnosis of Multiple Sclerosis

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Revisions to diagnostic criteria for MS in 2017 allowed CSF-specific oligoclonal bands (OCBs) to confirm diagnosis in individuals with clinically isolated syndrome (CIS) and evidence of dissemination-in-space (DIS).[1] We examined the impact that this change had on reaching a diagnosis of MS, when applied retrospectively to a population-based, real-life cohort of patients with CIS.

Records of 232 patients were reviewed who had experienced a CIS between August 2010-January 2015 and had at least 2 years of prospectively collected longitudinal data. We identified 102 patients who had MR imaging within 18 months of symptom onset, follow-up MRI within a further 18 months, and CSF examination as part of their diagnostic workup. The 2010 and 2017 revisions of the McDonald diagnostic criteria for MS were applied retrospectively to this cohort. Rates of conversion to clinically definite MS (CDMS, defined as a second clinical event) were also described.

Of 102 patients with CIS, 71 (70%) were female and mean age at symptom-onset was 36 years. The CIS presentation was monosymptomatic in 38 cases (15 optic neuritis, 14 pure sensory, 7 brainstem and 2 pure motor) and polysymptomatic in 64 cases. Overall 75 (74%) of individuals had positive OCBs. No patients received disease-modifying therapy (DMT) before fulfilling 2010 diagnostic criteria for MS.

During a mean follow-up period of 4.3 years (range 2.0 – 7.3), 88 (86%) individuals fulfilled 2017 criteria and 83 (81%) fulfilled 2010 criteria for the diagnosis of MS. Mean time to

diagnosis was 6.8 months and 9.3 months respectively (Tarone-Ware test,  $p=0.046$ ). Sixteen of 24 (67%) patients who fulfilled 2017 diagnostic criteria on the basis of CSF, went on to develop CDMS (mean follow-up 4.2 years, mean interval from CSF-examination to CDMS 11 months). In contrast, only 3 of 16 (19%) individuals who fulfilled 2017 criteria on the basis of radiological evidence of dissemination in time went on to develop CDMS (mean follow-up 4.0 years). However, 5 had received DMT post-diagnosis, which may have influenced time to CDMS. There was no difference in the survival distribution for reaching CDMS after radiological versus CSF-confirmation of MS diagnosis (Tarone-Ware test,  $p=0.165$ ).

Although possible bias in patient selection exists, our data support the premise for the 2017 revisions, which were aimed at expediting diagnosis without compromising diagnostic specificity. Previous authors have found that using radiological evidence for dissemination in time increases the sensitivity for less active MS.[2, 3] We found that the CSF-confirmation of diagnosis appeared at least equivalent to radiological dissemination-in-time in its predictive value of subsequent CDMS. Reducing diagnostic delay serves to alleviate uncertainty, facilitates discussions about prognosis, management and care needs, and may also reduce the time to receiving DMTs. Whether the 2017 McDonald criteria revisions should prompt wholesale change in the diagnostic pathway in centres that ordinarily perform few CSF-examinations should be considered. In conclusion, we found that the use of CSF examination to confirm the diagnosis of MS according to 2017 McDonald revisions appears to accelerate diagnosis in a real-world setting with CIS, without compromising existing standards of diagnostic accuracy.

The authors do not have any conflicts of interest.

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