Applying the 2017 McDonald Diagnostic Criteria for Multiple Sclerosis

Authors' reply

We thank Axel Petzold for highlighting the most significant change in the 2017 McDonald Criteria for multiple sclerosis (MS) compared to the 2010 Criteria, namely that in a patient with a typical clinically isolated syndrome and fulfillment of clinical or MRI criteria for dissemination in space, demonstration of cerebrospinal (CSF)-specific oligoclonal bands (OCBs) now allows a diagnosis of MS to be made.¹ As the case he provides illustrates, in the 2017 Criteria, the presence of CSF-specific OCBs in the appropriate setting substitutes for the requirement for demonstration of dissemination in time, allowing disease therapy to be initiated if indicated. This, in fact, was the intent of the revision. He correctly points out several important factors in the interpretation of CSF OCBs: appropriate specimen handling and analytic techniques, and analysis of paired CSF and serum samples to confirm that the OCBs are unique to CSF.² A final important point that Axel Petzold makes, and that Masoud Etemadifar and Fateme Sabeti also emphasize, is recognition that CSF OCBs are not specific for MS but can be used to support the diagnosis only when the overall CSF findings, other laboratory tests, and clinical features do not point to an alternative diagnosis.^{3,4}

Paulus Rommer and Uwe Zettl advocate incorporating CSF OCBs formally into the McDonald Criteria to demonstrate intrathecal antibody production and confirm an inflammatory disease process. The Panel addressed this point in its discussions but noted that CSF OCBs are neither completely specific nor sensitive for MS,⁴ particularly early in the disease process when diagnostic uncertainty is the most problematic. Thus, the Panel concluded not requiring specific findings on CSF examination to make the diagnosis in all cases. Nevertheless, as stated in our paper, clinicians should have a low threshold to undertake CSF analysis to increase diagnostic confidence when there is insufficient clinical and MRI evidence supporting a

diagnosis of MS; with a presentation other than a typical clinically isolate syndrome; with clinical, imaging, or laboratory features atypical of MS; and in populations in which MS is less common.

We thank Philipp Schwenkenbecher and colleagues for presenting data supporting the improved sensitivity of the 2017 McDonald Criteria compared to the 2005 and 2010 McDonald Criteria. This study contributes to the validation of the Panel's recommendations.

Elia Sechi and colleagues note that the 2017 McDonald Criteria for patients with a progressive course from onset were not changed from the 2010 McDonald Criteria, aside from including cortical brain MRI lesions in addition to juxtacortical lesions to make the diagnosis and that no distinction between symptomatic and asymptomatic MRI lesions is required. They indicate that with these changes some patients with so-called progressive solitary sclerosis⁵ may meet the diagnostic criteria for primary progressive MS, specifically, patients with a progressive course over one year, a supratentorial or infratentorial brain lesion characteristic of MS, and CSF-specific OCBs. While this is correct, a similar patient who has a single symptomatic lesion in the cervical cord, i.e. in an only slightly more caudal location, would not fulfill the criteria. The Panel noted this and other apparent inconsistencies in such special circumstances but, as indicated, we required any revisions to the Criteria be based on supporting data. Sechi et al's point deserves fuller exploration. We look forward to new data to inform further refinement of the Criteria, especially for patients with atypical presentations.

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