Active immunotherapy may delay disability in progressive MS

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In this issue of the journal, an epidemiological study using global multiple sclerosis (MS) database is published that investigated prognostic factors in advanced stages of MS. The cohort analysed included prospectively collected data of over 3000 patients with MS, and among various factors comprised demographics, age at onset, disease duration, annualised relapse rate, disability as rated by Expanded Disability Status Scale (EDSS) and history of immunotherapies. By dividing disease stage in three subgroups or 'epochs' as called by the authors (EDSS 3–6, 4–6 and 6–6.5) one of the relevant findings was that previous disease activity before entering advanced stages of MS had no impact on disease progression in later stages. Another important, and rather encouraging, finding was that active immunotherapy adjusted to the advanced demands does pose a delaying factor that prevents further progression. MS has been traditionally viewed as two-stage disease: beginning with relapses and remissions, and accumulating disability at advanced stages, with many facets of disease activity in between. This concept has proven useful from the clinicians’ standpoint as it allows the assessment of accessory assistance including symptomatic drugs and non-drug approaches that help ease the everyday difficulties of patients with MS with severe disabilities. However, despite growing evidence that inflammatory processes prevail throughout all stages of disease, the two-stage division has also supported the notion that only the earlier stage of MS with apparent disease activity suggestive of autoimmune inflammation such as clinical relapses and MRI lesions, is responsive to immunotherapy. In turn this two-stage divide tempers the conclusion that the latter, progressive stage of MS is mainly driven by neurodegeneration that is not accessible to any causal therapy. Hence, the paradigm that splits MS into inflammatory stage as opposed to degenerative stage excludes a large number of patients from potential disability delaying therapy. The current study proposes an alternative approach for assessing the disease stages of MS by analysing prognostic markers in the subgroups of advanced MS. Interestingly, the findings presented here partially contradict earlier epidemiological studies that had detected prognostic markers such as relapse rate, age, sex and certain symptoms for disease progression. Yet, the results also confirm more recent studies that suggest advanced MS stages being amnesic to early-stage characteristics such as relapse rate. The seeming discrepancy between the findings of previous studies and the more recent ones in the context of prognostic markers may be well explained by the fundamental difference in drug availability. While at the time when the millennium studies were conducted only two substance groups had been specifically approved for MS treatment, that is, β-interferons and glatiramer acetate, the number of drugs approved for the treatment of relapse remitting MS has more than quadrupled since then. In the realm of the ever-growing armamentarium of effective MS drugs—now adding to nine substance classes—the conclusions that neurologists involved in MS management can draw from the current study include: maintaining clinical vigilance in order to detect early signs of disease progression that mark advanced MS stages, and considering to withdraw the less-effective MS drugs and instead to deploy the so-called escalating immunotherapies. Amidst growing attention for the need to tackle progressive MS both in research efforts and clinical trials the core messages of the current study are really good news. They also encourage the MS community to apply recent advances in understanding MS aetiology to all stages of disease. These comprise environmental risk factors such as smoking and diet and targeting them may prove beneficial also in progressive MS.

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