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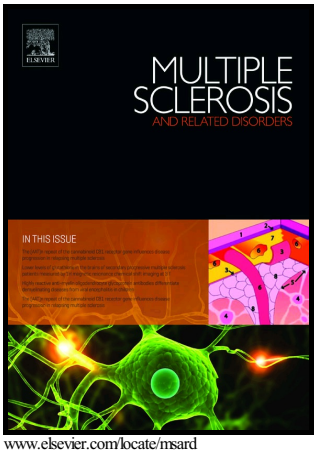

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The Evolution of "No Evidence of Disease Activity" in multiple sclerosis

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Abstract

The availability of effective therapies for patients with relapsing-remitting multiple sclerosis (RRMS) has prompted a re-evaluation of the most appropriate way to measure treatment response, both in clinical trials and clinical practice. Traditional parameters of treatment efficacy such as annualized relapse rate, magnetic resonance imaging (MRI) activity, and disability progression have an important place, but their relative merit is uncertain, and the role of other factors such as brain atrophy is still under study. More recently, composite measures such as "no evidence of disease activity" (NEDA) have emerged as new potential treatment targets, but NEDA itself has variable definitions, is not well validated, and may be hard to implement as a treatment goal in a clinical setting. We describe the development of NEDA as an outcome measure in MS, discuss definitions including NEDA-3 and NEDA-4, and review the strengths and limitations of NEDA, indicating where further research is needed.

Keywords: No evidence of disease activity; NEDA; multiple sclerosis; magnetic resonance imaging

Introduction

Multiple sclerosis (MS) is an inflammatory demyelinating disorder of the central nervous system that affects more than two million people worldwide, with disease onset typically between 20 and 40 years of age.(1) Relapsing-remitting multiple sclerosis (RRMS), the most common form of the disease, is characterized by the subacute onset of neurological deficits lasting at least 24 hours followed by at least partial recovery.(2) The pathological hallmark of MS is the formation of multifocal inflammatory demyelinating lesions, but significant neurodegeneration occurs due to irreversible axonal, neuronal, and synaptic loss that persists throughout the natural course of the disease.(3)

With major advances in the efficacy of MS disease modifying therapies (DMTs) over the past two decades, therapeutic goals are rapidly evolving. Rather than focusing solely on reducing relapse