No Evidence of Disease Activity (NEDA) over the long-term in patients with Relapsing Remitting Multiple Sclerosis

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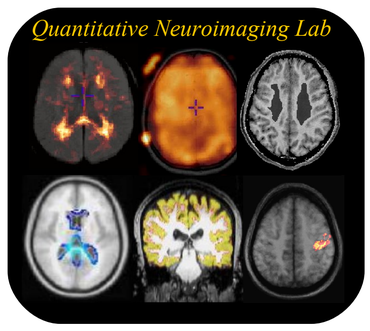


Background and Objective

NEDA is currently expressed as no evident active MRI lesions, no confirmed clinical relapses, and no confirmed disability progression as measured by the Expanded Disability Status Scale (EDSS); the MRI-derived brain volume loss (BVL) has been recently suggested as an additional, fourth component (*NEDA-4*).
Little data are available on the persistence of *NEDA* in the long-term (Rotstein DL, *et al.* JAMA Neurol*).*
We aim here to explore whether the status of "*no evidence of disease activity (NEDA)*" as evaluated by clinical and magnetic resonance imaging (MRI) findings can be found in the long-term in patients with relapsing-remitting (RR) multiple sclerosis (MS).

Material

We studied ninety-one patients (65 women and 26 men) with RRMS (mean age=34±8.4 years, mean disease duration=5.3±6 years, median EDSS=1.5,), who were recruited between January 2000 and May 2001 among those who were referring to the MS Clinics of the Universities of Siena and Florence, and the Hospital of Empoli. Patients underwent clinical and MRI examinations over 10 years. *NEDA* was described as no new/enlarging T_2 lesions on MRI, no confirmed clinical relapses and no confirmed EDSS progression and was assessed over 10 years.

Methods

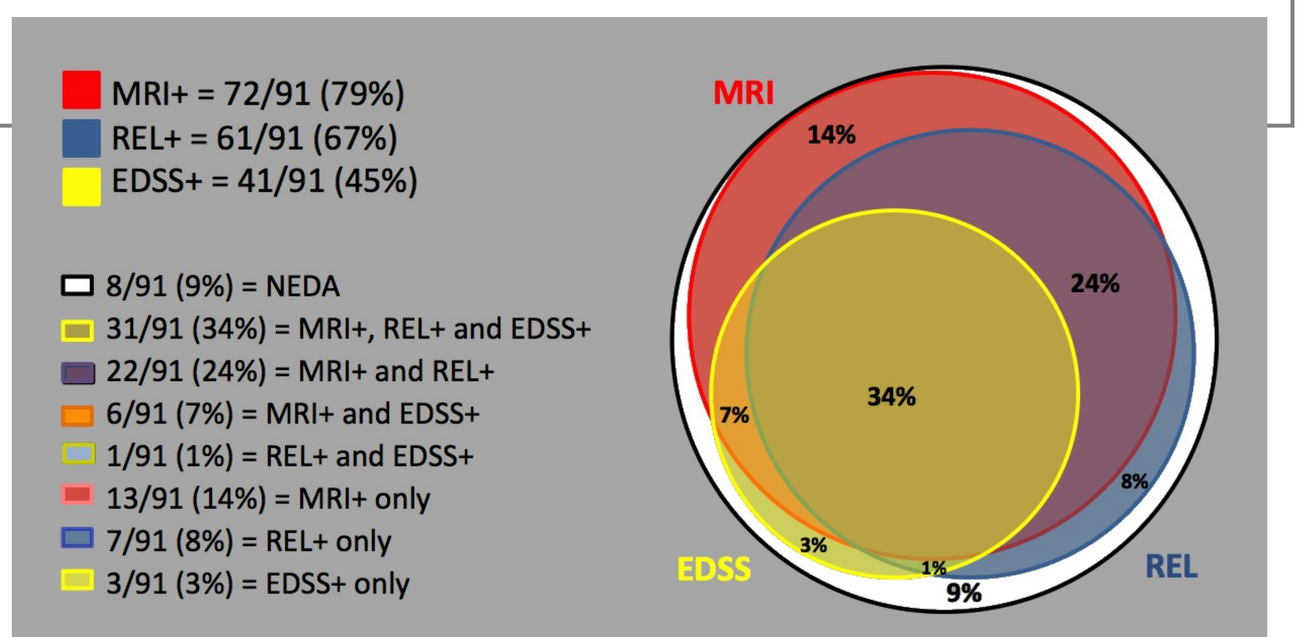
Brain MRIs were acquired using a 1.5 T Philips Gyroscan (Philips Medical Systems, Best, The Netherlands). All patients were examined using the same MR protocol, which included a dual-echo, turbo spin-echo sequence yielding proton density (PD) and T_2-weighted images for assessment of brain lesions and T_1-weighted images for measurement of BVL, which was estimated by using the SIENA method.
During the 10 years, 82/91 patients were treated with current disease-modifying therapies (DMTs).

Results

After 10 years, there were 19/91 RRMS patients free from MRI activity (21%), 30/91 (33%) free from relapses, and 50/91 (55%) without sustained EDSS progression. There were 34/91 (37%) without significant BVL. Patients with *NEDA* were 8/91 (9%) and patients with *NEDA-4* were 5/91 (6%).

Discussion

The study extends previous work providing compelling evidence that *NEDA* rarely persists in the long term in a real-world cohort of RRMS patients. This is even more evident when BVL is included in the *NEDA* definition (i.e., *NEDA-4*). *NEDA* remains a very interesting outcome for clinical trials, but it might not be a realistic goal in clinical setting with current DMTs.



Red, blu and yellow circles represent, respectively, patients with evidence of new MRI lesions (MRI+), clinical relapses (REL+) or sustained disability progression (EDSS+). Circles with mixed colors represent patients with evidence of disease activity in more than one outcome measure. The white circle represents the remaining *NEDA* patients.

References

◆Havrdova E, Galetta S, Stefoski D, Comi G. ***Freedom from disease activity in multiple sclerosis***. *Neurology.* Apr 27 2010;74 Suppl 3:S3-7.

◆Nixon R, Bergvall N, Tomic D, Sfikas N, Cutter G, Giovannoni G**.** ***No evidence of disease activity: indirect comparisons of oral therapies for the treatment of relapsing-remitting multiple sclerosis.*** *Adv Ther.* Nov 2014;31(11):1134-1154.

◆Rotstein DL, Healy BC, Malik MT, Chitnis T, Weiner HL. ***Evaluation of no evidence of disease activity in a 7-year longitudinal multiple sclerosis cohort.*** *JAMA Neurol.* Feb 1 2015;72(2):152-158.