

Identification of Benign Multiple Sclerosis Using Whole Brain N-Acetylaspartate

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Introduction:

Multiple sclerosis (MS) is a progressive, autoimmune disorder that is characterized by demyelination and neurodegeneration. The most common clinical classifications are relapsing-remitting (RR-MS) (25%), secondary-progressive (40%), primary-progressive (15%), and benign (B-MS) (20%) (1). B-MS is characterized by an extended disease course with a relative paucity of clinical symptoms, often measured by the expanded disability status scale (EDSS). Occasionally, this form is discovered only at autopsy, which is in stark contrast to other more aggressive forms of the disease, which may lead to death within weeks of onset. Past studies that have described patients as benign have been retrospective in nature, and the clinical definition currently accepted to classify a patient as benign is a clinically definite disease duration of 15 years or more with an EDSS less than or equal to 3. However, to date, no study has been able to properly predict disease course in patients at diagnosis. In this study, we address this issue by comparing whole-brain *N*-acetylaspartate concentration (WBNA) in MS patients who are suspected to have a benign form with those that are suspected to have more aggressive forms of the disease. We hypothesize that patients with benign MS, on average, have higher concentrations of WBNA both of other MS patients as well as healthy normal controls.

Methods:

Absolute whole-brain NAA amount was obtained with non-localizing proton MR spectroscopy from 44 subjects, (14 men, 30 women) 44.7 ± 7.3 years old that have been diagnosed with B-MS (disease duration ≥ 15 years, EDSS ≤ 3.0). The amount was converted into WBNA dividing by their brain's parenchymal volume obtained from MRI image segmentation (2).

Results:

A regression plot of the WBNA of B-MS patients versus their disease duration is shown in Fig. 1 bottom. Included in the figure are the linear relationships in three different subgroups of RR-MS patients (stable, moderate, and rapid) as previously reported (3). The best fit line for the B-MS group is $y = -0.17x + 11.85$ ($R^2 = 0.18$) which is consistent with that previously reported for the moderately declining group. The WBNA loss per year is shown in Fig. 1, top. The average rate of decline is 0.33 mM/year and is tightly clustered within a limited range (-0.08 – 0.66 mM/y). There was no correlation between WBNA concentration and EDSS, T2W lesion volume, NBV, atrophy, age or disease duration.

Discussion:

Unfortunately, the data has dispelled our original hypothesis and it appears that patients with benign MS have WBNA levels that are indistinguishable from those with a conventional relapsing-remitting course; therefore, WBNA may not be a tool for forecasting disease progression, at least in this subset of MS patients. Since there was no correlation in the classical clinical metrics mentioned above, the only difference between patients with a benign course and a more moderate course is clinical performance, which indicates there are underlying issues of brain plasticity and compensatory mechanisms to which this technique is insensitive and nonspecific.

References:

1. Filippi, et. al. *Neurology* (1999), 52(3):588-94.
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3. Gonon, et. al. *Radiology* (2002), 225(1):261-8.

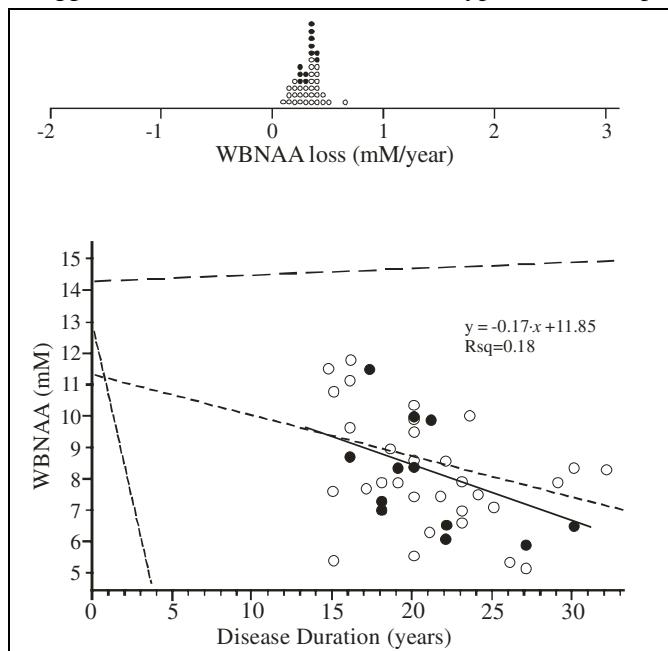


Fig. 1. Patients with suspected benign MS in the context of WBNA loss rate per year and the three classifications of multiple sclerosis course (stable, moderate, rapid). Filled circles indicate medicated patients.