Whole Brain N-acetylaspartate Concentration as a Surrogate Marker for Benign Multiple Sclerosis

D. Rigotti[1], T. Oberndorfer[1], J. Babb[1], C. Markowitz[2], J. Herbert[1], O. Gonen[1]

[1]Radiology, NYU School of Medicine, New York, NY, United States, [2]Neurology, UPenn Medical Center, Philadelphia, PA, United States

Introduction:

Multiple sclerosis (MS) is a progressive, autoimmune disorder that is characterized by demyelination and neurodegeneration. The most common clinical classifications are relapse-remitting (25%), secondary-progressive (40%), primary-progressive (15%), and benign (20%)(1). Benign 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, asserting that a patient that has a certain change in clinical symptoms over a long period of time may have a benign form of MS. 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 (WBNAA) in MS patients who are suspected to have a benign form with those that are suspected to have a more aggressive forms of the disease. We intend to show that patients with benign MS, on average, have higher concentrations of WBNAA 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 49 subjects that have been diagnosed with MS (13 men, 36 women) 38.6±7.4 years old. The amount was converted into WBNAA dividing by their brain's parenchymal volume obtained from MRI image segmentation (2).

Results:

The average WBNAA concentration for patients suspected to have benign MS was 14.51±0.7mM which was significantly different than those with more malignant forms of MS (9.93±2.02) and also higher than previously reported values for healthy normal controls (2). Fig. 1 depicts of three different classifications of MS ("stable", "moderate" and "rapid") based upon WBNAA concentration versus disease duration (3). Patients with suspected benign MS (based upon clinical symptoms, n=10) have been plotted and are almost exclusively among the "stable". All other MS patients (based on clinical symptoms, n=39) fall either in the "moderate" or "rapid" (data not shown). A box plot is shown in the inset of Fig. 1. It shows a significant difference between patients with suspected benign MS versus those with more malignant forms of MS.

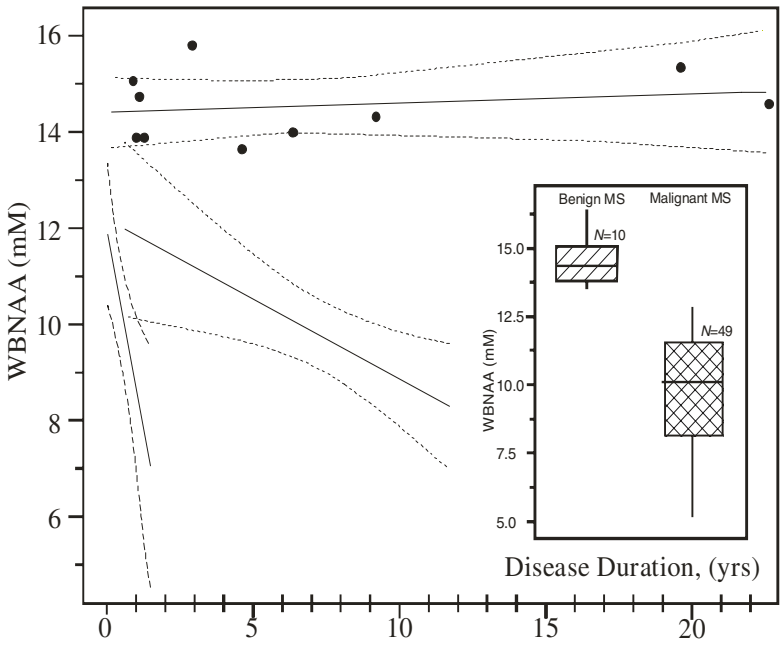

Fig. 1. Patients with suspected benign MS in the context of three classifications of MS course ("stable", "moderate" and "rapid"). Box plots (inset) of 1st, 2nd (median) and 3rd quartiles to 95% (whiskers) of WBNAA concentration of patients with suspected benign MS vs. those with more malignant disease course.

Discussion:

The chief result from this study is that 20% of MS patients who go on to have a benign disease course appear to have WBNAA concentrations higher than not only other MS patients, but also normal healthy controls. This study also describes the potential role of WBNAA as a surrogate marker for differentiating between different forms of MS. An important conclusion reached is that it may be possible to triage, at initial diagnosis, those patients with benign MS by simply measuring the WBNAA concentration.

References:

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