

Serial Whole-Brain N-acetylaspartate Concentration in Multiple Sclerosis Patients

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Introduction:

Multiple sclerosis (MS), the most prevalent demyelinating neurological disorder, is the primary cause of non-traumatic disability in young and middle-aged adults. Because the irreversible effects of MS are thought to be chiefly caused by neuronal loss, surrogate markers specific for the viability and concentration of these cells correlate better with clinical disability and might predict a better outcome. One key ¹H-MRS-detectable metabolite is *N*-acetylaspartate (NAA), which is almost exclusive to neurons and therefore considered a good marker for their concentration and health. Previous studies measuring whole-brain NAA (WBNA) concentration, cross-sectionally, have shown it to be a robust surrogate marker for diffuse neuronal loss and dysfunction.

Moreover, WBNA has been shown to be stable in young healthy controls both at multiple sites (1) over a period of four years (2). Since many diseases studied with ¹H-MRS, including MS, are chronic, it is frequently part of a serial study of one to two years; therefore it is important to conduct serial follow-ups to more accurately measure WBNA concentration in this timeframe. To address this issue, we report results from a serial study of the WBNA concentration in newly diagnosed MS patients.

Methods:

Absolute whole-brain NAA amount was obtained with non-localizing proton MR spectroscopy (3) at 6-month intervals from 19 newly diagnosed (disease duration 48±19 months) relapsing-remitting MS subjects (5 men, 14 women) 33.5±5.0 years old and 10 age-matched controls. The absolute whole-brain NAA amount was converted into WBNA concentration by dividing by their brain's parenchymal volume obtained from MRI image segmentation. All subjects gave written IRB approved informed consent.

Results:

Results are summarized in Fig. 1. The mean patient WBNA at baseline was 9.8±1.4 mM, 9.2±1.5 mM at first follow-up and 8.9±1.6 mM at second follow-up, which was significantly less than that measured for controls (11.7±0.9). There was no significant change in BV over the course of the study. There was no significant difference in terms of the within-subject change in either WBNA or BV with respect to gender, age, disease duration or medication.

Discussion:

This is the first time that quantifiable changes that reflect ongoing pathogenesis have been measured in MS patients using the WBNA methodology. While the specific cause and mechanism of NAA loss remains uncertain, it is clear that it is a result of ongoing disease activity, resulting in neuronal loss and/or dysfunction. Since this decline is quantifiable in a much shorter period of time compared to discernable clinical changes (measured by EDSS, etc.) which can take much longer to manifest clinically, the outcome of this study may indicate that WBNA avails the neurologist a more sensitive “feedback” mechanism for the efficacy of treatment and the course of individual patients.

References:

1. Benedetti, *et.al. AJNR*, 28:72
2. Rigotti, *et.al. AJNR*, 28:1650
3. Gonen, *et.al. Neurology*, 11:54

