Cognitive dysfunction lateralizes with NAA in multiple sclerosis

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Introduction

Multiple sclerosis (MS) is a CNS disorder characterized by repeated cycles of white matter damage, recovery and injury. Accurate assessment of the degree of axonal integrity and damage is important. The most commonly used outcome measures in MS are the EDSS (expanded disability status scale) and MRI. The EDSS is limited because it emphasizes ambulation (1,2). Axonal integrity can be directly assessed by N-acetyl aspartate, NAA. Creatine (Cr) is found in high concentrations in glia. Although NAA/Cr is useful to describe gliotic reaction and neuronal loss, its application in MS may be less sensitive. The reactionary Cr changes may occur late in the disease process, whereas NAA is more dynamic, reflecting the degree of demyelination and remyelination. Our goal was to determine the relationship between cognitive function, EDSS, and NAA levels. Periventricular NAA is evaluated since previous studies have found this area to be chronically involved with MS (3,4). As many cognitive functions are relatively lateralized, we quantified measures of right and left hemisphere periventricular NAA.

Methods

Clinical: 19 patients (8 women, 11 men) were recruited from the SUNY Stony Brook Comprehensive MS Clinic. Mean age was 44±9.3y, with a range from 24-60yr. They were clinically described as relapsing remitting (n=7), secondary progressive (n=7), and primary progressive (n=5). EDSS scores ranged from 1.0-6.5, mean 3.3±1.5. Cognitive functioning was assessed by a modified version of the Brief Repeatable Battery (BRB, 1) with measures selected to represent a range of cognitive functions. These tests included the Selective Reminding Test (verbal memory, left hemispheric) and the Tower of Hanoi (conceptual planning, more right hemispheric).

MR: A Varian Siemens 4T Inova system and volume head coil was used. Inversion recovery gradient echo scout images were obtained to determine the midline sagittal plane. The 1cm slice of interest was defined symmetrically orthogonal to the line defined by the posterior and anterior aspects of the corpus callosum. The spectral data were acquired with TE 50ms, TR2s spin echo. 2D phase encoding was applied (24x24) on a field of view of 190mm, giving a nominal spatial resolution of 0.64mm. Quantification was performed using a water spectroscopic image taken through the ventricles. Ventricular CSF content was assumed IIOM, with a T2 spectral data were acquired with TE 50ms, TR2s spin echo. 2D phase encoding was applied (24x24) on a field of view of 190mm, giving a nominal spatial resolution of 0.64mm. Quantification was performed using a water spectroscopic image taken through the ventricles. Ventricular CSF content was assumed IIOM, with a T2

Fig. 1 shows a segmented scout image and spectra from a patient with secondary progressive MS

Conclusions

We have combined cognitive testing with quantitative MR spectroscopic imaging to evaluate the relationship between cognitive function with concentration of periventricular NAA in MS patients. These findings show a strong relation between lateralized PV NAA and measures of right and left hemisphere cognitive function. Given the prevalence of lesions in periventricular tissue with MS, we interpret the PV NAA measurements to be a manifestation of chronic disease activity. That these measurements correlate with cognitive function reflects the local neurological function of these regions and a general evaluation of disease activity.

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References

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