3D Proton Spectroscopy of Gray Matter Nuclei in Relapsing Remitting MS

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Introduction

GM involvement at cortical and sub-cortical level in MS is gaining increased recognition (1).Despite evidence of basal ganglia (BG) pathology at *post mortem* examination (2), most of the *in vivo* magnetic resonance (MR) studies using T2-weighted images (T2WI) and quantitative techniques, such as magnetization transfer (MT) and diffusion tensor (DT) imaging have failed to detect significant abnormalities in BG of MS patients (3) ^{1}H-MRS permits non-invasive assessment of neuronal, axonal and membranes health through assessment of NAA, Cho and Cr levels.While neurodegenerative MS pathology of the thalamus has been well described in a recent study of *in vivo* spectroscopy and histopathology, the single-voxel methodology used excluded the BG (6). This elegant study motivated our use of three dimensional (3D) ^{1}H-MRS to compare all the deep GM nuclei metabolites' levels of RR MS patients with controls and investigate relations between these levels and neurological deficits.

Methods

Eleven RR MS patients (8 women) of mean age 39 (range: 26-48) years, EDSS score 2.5 (range 0.0-6.0) and 9 age- and sex-matched controls underwent the same MRI and 3D ^{1}H-MRS procedure at 1.5 T. Contiguous axial, sagittal and coronal T1WI spin-echo (TE/TR=15/450 ms) and axial T2WI dual spin-echo (TE_1/TE_2/TR=16/90/2500 ms) 7.5 mm thick slices were obtained at 240^2 mm^2 field-of-view (FOV) 256^2 matrices. A 3D ^{1}H-MRS sequence TE/TR=135/1600 ms which excited an image-guided $8_{LR}\times10_{AP}\times6_{IS}$ cm^3 left-right (LR) × anterior-posterior (AP) × inferior-superior (IS) volumes of interest (VOI), as shown in Fig. 1 and partitioned it into $8_{LR}\times10_{AP}\times8_{IS}$ =640 voxels 0.75 cm^3 each(4). The data was zero-filled from 1024 to 2048 in the time and from 16×16 to 128×128 in the spatial domains and reconstructed. Absolute NAA, Cr and Cho concentrations were obtained in each voxel with phantom replacement. For each subject, an axial T1WI showing the thalamus, head of caudate, lentiform nucleus, as shown in Fig. 1. Our custom software transcribed the manually drawn contours of each nucleus, onto the corresponding regions of the three metabolic maps and computed the average spectrum, and three metabolic levels ± their standard deviation from each drawn region.

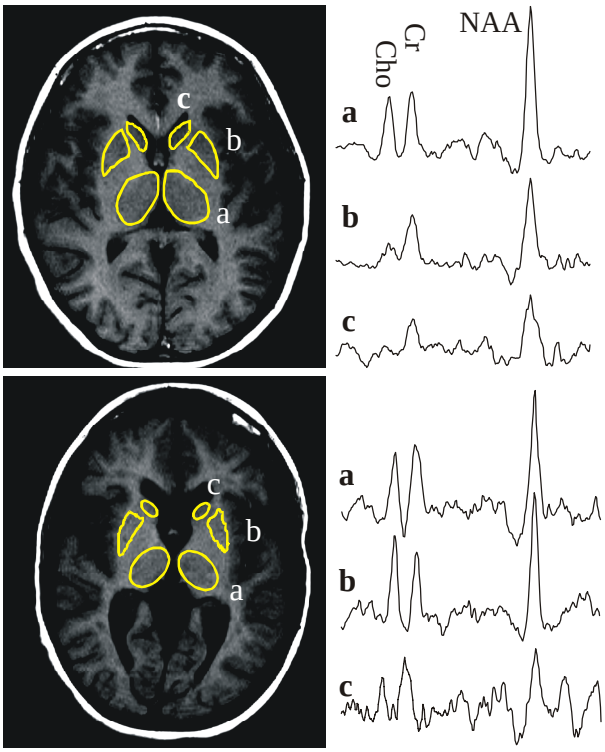

Fig. 1: Left T1-weighted MRI of analogous slices in a control (top) and RR MS patient (bottom). The deep GM nuclei: Thalamus (a), lentiform (b) and caudate (c) are outlined. Right: corresponding average spectra from these regions and the metabolite levels are in the text.

Results

There was no significant difference between the left and right side for any of the deep GM nuclei and age was not significantly associated with [NAA], [Cr] and [Cho]. The mean±SD concentration of NAA in the deep GM was significantly lower (8.85±2.18 mM) whereas the concentration of Cho was significantly higher (2.16±0.55 mM) in patients compared to controls (9.50±1.97 mM, 1.86±0.47 mM; p=0.02 for both) No significant difference was found with regard to the concentration of Cr between patients (6.43±1.53 mM) and controls (6.51±1.62 mM). No correlation was found between metabolite concentrations and either disease duration or EDSS.

Discussion

GM lesions are frequently missed on T2W scans due to their small size and the poor contrast resolution with the surrounding GM. 3D ^{1}H-MRS is a useful tool for assessing the burden of disease from several deep GM structures in the same unit time. NAA decrease might reflect neuronal loss or dysfunction due to the effect of distant WM lesions or to local microscopic foci of inflammation. This is in line with the concomitant increase of the Cho level which reflect membrane turnover and hypercellularity typical of inflammatory processes.

References

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