Global Magnetization Transfer Imaging Demonstrates Spinal Cord Changes in Patients with Adrenomyeloneuropathy

S. A. Smith[1,2], S. A. Fatemi[3], K. M. Zackowski[4], A. J. Bastian[4], P. C. van Zijl[1,2], G. V. Raymond[3,5], H. W. Moser[3,5], X. Golay[1,2]

[1]Radiology, Johns Hopkins University, Baltimore, Maryland, United States, [2]F.M. Kirby Research Center, Kennedy Krieger Institute, Baltimore, Maryland, United States, [3]Neurogenetics Research Center, Kennedy Krieger Institute, Baltimore, Maryland, United States, [4]Motion Analysis Laboratory, Kennedy Krieger Institute, Baltimore, Maryland, United States, [5]Neurology, Johns Hopkins University, Baltimore, Maryland, United States

Introduction

The evaluation of Adrenomyeloneuropathy (AMN), a neurodegenerative disease, is hampered by lack of sensitive and quantitative markers. Pathological changes in AMN, characterized by a distal axonopathy, are mainly confined to the spinal cord; specifically the ascending dorsal columns in the cervical regions and the cortical spinal tracts in the lumbar spine (1). Spinal cord assessment in AMN is difficult since the small diameter of the spinal cord and its proximity to surrounding bone and cerebrospinal fluid (CSF) hamper *in vivo* visualization and quantitative evaluation. Conventional MRI detects only spinal cord atrophy in the late stage of AMN due to the absence of inflammatory lesions. It is however insensitive to white matter abnormalities in AMN (2). A Magnetization Transfer (MT) based imaging approach, referred to as Global MT (GMT) was devised to achieve a high resolution, quantitative assessment of spinal cord white matter. MT-based imaging was chosen since it is sensitive to small changes in CNS pathology (3, 4).

Methods

MR examinations were performed on ten men with AMN (severely symptomatic), ten women heterozygous for X-ALD (mildly symptomatic), and nine age-matched volunteers, after written informed consent. All studies were performed on a 1.5-T Philips Intera-NT system (Philips Medical systems, Best, The Netherlands). Quadrature body coil, transmission, and a two-element phased array coil, reception, were used. Flow-insensitive MT-weighted images were acquired using a spoiled 3D-Gradient Echo (3D-GRE), TR / TE /α = 50 ms / 13 ms / 7°, with a five-lobed sinc MT pre-pulse of 15 ms. Ten RF offsets were logarithmically sampled between 1 and 63 kHz, plus a reference scan (0° MT pre-pulse). Field of view = 225x225x48 mm, matrix = 512x512x32, total scan time 33 minutes. Signal normalization was achieved using a ROI manually selected within CSF in the reference scan for all slice. The GMT was then defined as the integral of the CSF normalized MT spectrum from 1 - 63 kHz. The cervical segment, C1 – C3 was defined by a high resolution Steady State Free Precession (SSFP) optimized for the detection of the nerve roots (TR/TE/α = 5.3 ms / 2.7 ms / 45°). All other parameters for SSFP were the same as the MT sequence; scan time = 2 minutes. The highest slice for all scans was at the level of the foramen magnum. The Mean GMT value of an ROI manually selected from within the dorsal column of each slice was evaluated to assess disease severity. Unpaired t-tests were performed to detect significant differences in the mean GMT value between controls, the severely affected men, and less severely affected women.

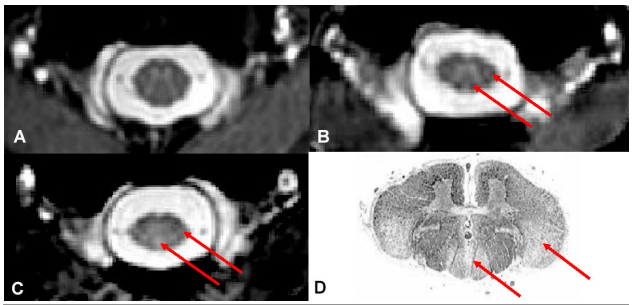

Figure 1: GMT Images at C2 of: A) Healthy Volunteer, B) Mildly symptomatic AMN patient, C) Severely symptomatic AMN patient, D) Post-mortem of cervical spinal cord (with permission, ref. 1).

Results and Discussion

Figure 1 shows GMT images of A) normal volunteer, B) mildly symptomatic patient, C) severely affected patient. Post-mortem pathology (1D) shows loss of myelin staining in lateral and dorsal columns (1) agreeing with GMT hyperintensities (arrows). Good grey-white contrast is appreciated in all slices, especially in visualizing the grey matter horns (butterfly-shaped), which separate the lateral and dorsal columns (dark). Note that myelinated white matter is dark, the grey matter is less dark and the CSF is bright white on GMT images. Figure 2 shows mean GMT signal (in kHz) of the dorsal column plotted for each slice. Slice 1 corresponds to C3 and slice 25 corresponds to C1 as delineated by the SSFP sequence. Significant differences were seen in the mean dorsal column GMT value between the more severely affected patients (t – value = 11.3, $p < 0.0001$), less severely affected patients (t – value = 4.3, $p < 0.0006$) and the control mean. In this study, the CSF was chosen from the reference scan, but since the CSF should contain no MT effect, a higher SNR could be achieved by defining an ROI in the CSF from each slice of each MT weighted scan, eliminating then at the same time the need for a reference acquisition. In AMN, it was unclear which offset frequencies are most sensitive to pathological changes, thus the GMT can be used to survey the MT spectrum to determining the frequencies most sensitive to any specific neurodengerative disease.

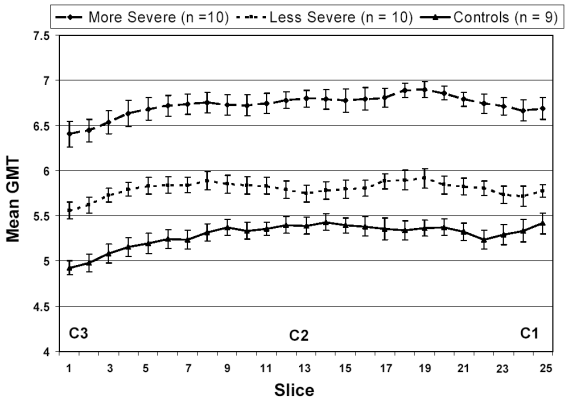

Figure 2: Mean dorsal column GMT values for severely affected patients (dashed), less severely affected patients (dotted), and healthy volunteers (solid). GMT values reported in kHz.

References

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Abstract

The evaluation of Adrenomyeloneuropathy (AMN), a neurodegenerative disease affecting the spinal cord, is hampered by lack of sensitive markers. Global Magnetization Transfer (GMT) in which MT images are acquired over a wide frequency range, was employed to assess white matter pathology in the spine of AMN patients. Studies were conducted in ten severely affected men, ten less severely affected women and ten controls. GMT images showed signal hyperintensities in lateral and dorsal columns of all patients, which agrees with pathological studies. Mean GMT signal in the cervical dorsal column showed highly significant differences between the affected men, women and controls.