MRS and diffusion MRI of the spinal cord in Friedreich's Ataxia

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Target Audience: neurologists, neuroradiologists, and MR physicists interested in ^{1}H MRS and DWI of spinal cord.

Purpose

Friedreich's ataxia (FRDA) is a degenerative syndrome characterized by neuromuscular dystrophy, cardiomyopathy and spinal cord atrophy[1]. A hallmark of the disease and early event in the pathogenesis is substantial demyelination and gliosis of the posterior and lateral columns of the spinal cord, likely occurring prior to cerebellar pathology. As such, imaging and spectroscopy of the spinal cord may yield relevant and much needed biomarkers at early stage. However, there have been very few MR studies of the spinal cord in patients with FRDA[2], and, to our knowledge, none using ^{1}H MRS or DTI, due in part to technical challenges (B_0 shim, motion artifacts). Here, our objective was to characterize neurodegeneration in early stage patients with FRDA using ^{1}H MRS and DTI of the spinal cord.

Methods

We studied 15 patients and age-matched controls. All measurements were performed on a Siemens Trio 3T scanner (Siemens, Erlangen, Germany). The standard body coil was used for RF transmission while the neck matrix and spine matrix were used for signal reception. In addition, the 12-channel head matrix (bottom part) was also used for reception for MRS while the body matrix coil was used for diffusion MRI. Cardiac-triggered ^{1}H MR spectra (T_E = 28 ms, T_R = 5 s, 256 averages) were acquired in the spinal cord using a modified semi-LASER sequence[3] in an $8 \times 6 \times 30$ mm^3 voxel positioned along C4-C5 vertebrae. Spectra were quantified with LCModel using water as an internal reference. Diffusion MRI was acquired using a readout-segmented echo-planar sequence[4] with the following parameters: TR/TE = 4500/66ms; voxel size = 1.1x1.1x3.3mm^3; iPAT=2; 30 axial slices; 30 diffusion gradients with *b*-value= 800 s/mm^2 and 6 additional *b*=0 volumes. Diffusion MRI was acquired in two opposite phase encoding directions (A-P and P-A) and combined to correct for geometric and eddy current distortions[5]. All subjects were also assessed by the Friedreich's Ataxia Rating Scale (FARS), which yields a composite ataxia score in the range of 0 (no ataxia) – 159 (most severe ataxia).

Results

Patients had FARS scores averaging 51±20 (mean ± SD, range 10-81) and age 20±7 years (range 11-32). We observed ~40% lower NAA ($p < 0.005$) and ~46% higher myo-inositol ($p < 0.001$) levels in spinal cord of patients vs controls (Fig. 1), reflecting neuronal damage and gliosis. These neurochemical concentrations correlated with FARS scores (NAA $R^2 = 0.43$, $p < 0.005$; mIns: $R^2 = 0.19$, $p < 0.01$). DTI data showed strong differences in the integrity of the axonal pathways within and leaving the spinal cord (nerve roots) (Fig. 2). Consistent with known spinal atrophy in FRDA[2], fractional anisotropy was lower in the cervical spinal cord of patients (Fig. 2, FA = 0.47 in patient vs. 0.61 in control, spinal cord volume = 0.56 ml in patient vs. 0.75 ml in control, measured on 3 axial slices around C2).

Discussion and Conclusion

This is, to our knowledge, the first report using ^{1}H MRS or DTI to study spinal cord in patients with FRDA. All data were acquired at 3T using a widely available clinical system and newly developed sequences. A few previous ^{1}H MRS studies have shown relatively small changes in the brain with ^{1}H MRS in patient populations with more severe symptoms[6,7]. Similarly, previous MRI studies have shown changes in the brain using T_1-weighted MRI[8] and diffusion MRI[9-11]. The fact that we observed large changes in the cervical spinal cord of early-stage patients is consistent with neurodegeneration onset occurring early in the spine. Such multi-modal MRI/S measurements in the spinal cord may yield further insight into disease mechanisms and provide markers of neurodegeneration in patients at an early stage to assess therapeutic efficacy in clinical trials.

References:
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Funding: NIH grants P41 EB015894, P30 NS5076408,the Friedreich's Ataxia Research Alliance and the Bob Allison Ataxia Research Center.

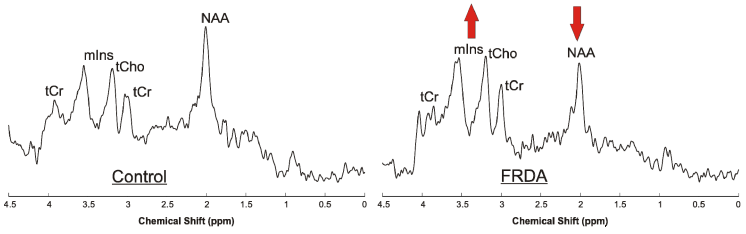

Fig 1. *MR spectra of the spinal cord (C4-C5) showing lower NAA and higher mIns in age-matched patient (right) vs control (left). Note the sharply different NAA / mIns ratio. Creatine concentration was unchanged.*

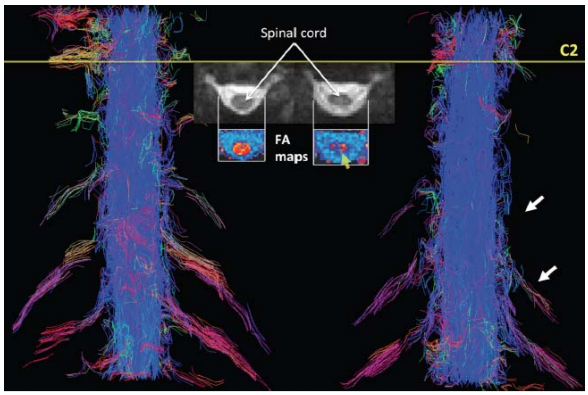

Fig 2. *Diffusion MRI of the spinal cord showing alteration of the nerve roots (white arrows) in age-matched patient (right) and control (left). Cord atrophy was visualized and quantified using fractional anisotropy (FA) maps (center images depicting axial slices through C2), which correlate with white matter integrity. Lower values (blue colors in the center FA maps) can be seen in the spinal cord for the patient's data (yellow arrow).*