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

Pierre-Gilles Henry1, Dinesh Deelchand1, Isabelle Iltis1, Diane Hutter1, Khalaf O Bushara1, Galin Ozt2, and Christophe Lenglet1
1Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, MN, United States

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

Purpose
Friedreich’s ataxia (FRDA) is a degenerative syndrome characterized by neuromuscular dystrophy, cardiomyopathy and spinal cord atrophy1. 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 FRDA2 and, to our knowledge, none using 1H MRS or DTI, due in part to technical challenges (B0 shim, motion artifacts). Here, our objective was to characterize neurodegeneration in early stage patients with FRDA using 1H 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 1H MR spectra (TE = 28 ms, TR = 5 s, 256 averages) were acquired in the spinal cord using a modified semi-LASER sequence3 in an 8 × 6 × 30 mm3 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 sequence4 with the following parameters: TR/TE = 4500/66ms; voxel size = 1.1x1.1x3.3mm3; iPAT=2; 30 axial slices; 30 diffusion gradients with b-value= 800 s/mm2 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 distortions5. 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 R2 = 0.43, p < 0.005; mIns: R2 = 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 FRDA2, 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 1H 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 1H MRS studies have shown relatively small changes in the brain with 1H MRS in patient populations with more severe symptoms6,7. Similarly, previous MRI studies have shown changes in the brain using T1-weighted MRI and diffusion MRI8-11. 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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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).