Diffusion and magnetization transfer imaging detects spinal cord lesions in amyotrophic lateral sclerosis

P-F. Pradat[1], J. Cohen-Adad[2,3], M. Elmendili[2], S. Lehericy[4], S. Blancho[5], V. Meininger[6], S. Rossignol[7], and H. Benali[2]

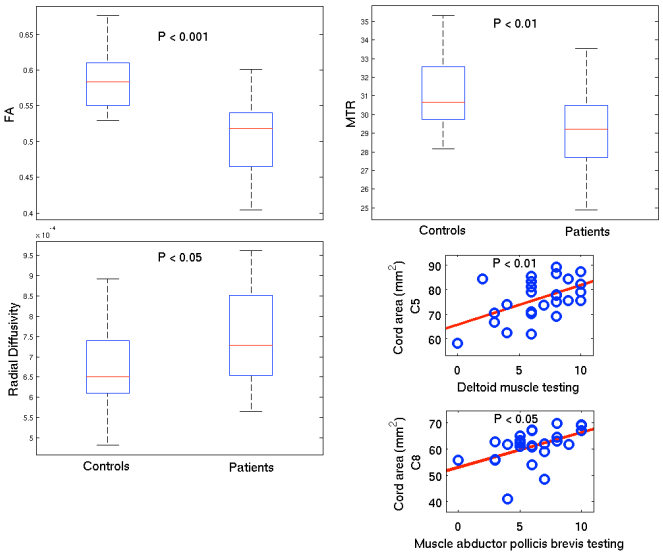
[1]Département des Maladies du Système Nerveux, Hôpital de la Pitié-Salpétrière, Paris, Paris, France, [2]UMR-678, INSERM-UPMC, Pitié-Salpêtrière Hospital, Paris, France, [3]A.A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA, United States, [4]Centre for Neuroimaging Research (CENIR), CRICM,INSERM U975, CNRS UMR 7225, Pitié-Salpêtrière Hospital, Paris, [5]Institut pour la Recherche sur la Moelle Epinière et l'Encéphale, France, [6]Département des Maladies du Système Nerveux, Pitié-Salpêtrière Hospital, France, [7]GRSNC, Faculty of Medicine, Université de Montréal, Montreal, Canada

Introduction. Amyotrophic lateral sclerosis (ALS) is a fatal degenerative disease characterized by involvement of both upper motor neuron, *i.e.*, cortico-spinal tract (CST), and lower motor neuron. Characterizing *in vivo* spinal lesions in ALS is crucial to explore the anatomic structures affected by the disease more precisely. Novel imaging techniques such as diffusion-weighted (DW) and magnetization transfer (MT) imaging provide sensitive markers of white matter pathology [1, 2]. In this study we combined for the first time DW, MT imaging and atrophy measurements to evaluate the cervical spinal cord of ALS patients.

Methods. Subjects. Patients with ALS (N = 26, age = 49±13 years) and age-matched controls (N=15) were recruited for this study. Patients were clinically assessed and scored on manual muscle testing (MRC score) the day of MRI acquisition.
Data acquisition. Subjects were scanned using a 3T MRI system (Tim Trio, Siemens Healthcare) using a combination of head, neck and spine receive coils (19-channel in total). Imaging protocol was: T2-weighted 3D turbo spin echo with slab selective excitation pulses (*52 sagittal slices, FOV=280mm, TR/TE=1500/120ms, 0.9x0.9x0.9mm^3, flip angle=140°, R=3 acceleration factor, BW=744Hz/Px*), DW imaging (*axial orientation, FOV=128 mm, TR/TE=700/96ms, 1x1x5mm^3, R=2, 64 diffusion directions, b-value=1000s/mm^2, BW=1086Hz/Px, echo spacing=1.04ms, 4 averaging, cardiac gating, advanced shimming*) and T1-weighted sequence with and without MT pulse (*axial orientation, FOV=230mm, TR/TE=28/3.2ms, 0.9x0.9x2 mm^3, flip angle=23°, BW=400Hz/Pix, Gaussian MT pulse: duration=9984μs, frequency offset=1200 Hz*).
Data processing. Cord sectional sizes were measured from the T2-weighted image at vertebral levels C4, C5, C6 and C7 using a semi-automatic method [3]. DW data were corrected for motion and diffusion tensor imaging (DTI) were estimated using FSL [4]. MT ratio (MTR) was computed voxel-wise using the T1-weighted image without (S_0) and with (S_{MT}) MT pulse as follows: $[(S_0 - S_{MT}) / S_0] \times 100$. Manual ROIs were drawn in the spinal cord to isolate ventro-lateral segments. DTI metrics and MTR were quantified in the ventrolateral spinal cord of each individual.
Statistics. Differences between controls and patients for: fractional anisotropy (FA), axial and radial diffusivities, mean diffusivity (MD), MTR, T1- and T2-weighted signals (normalized by CSF) and cord area were evaluated using two-tailed Student's t-tests two-way. ANOVA was performed to study how cord atrophy depends on the population (patient versus control) and the vertebral level (C4 to C7). Pearson's correlation between muscle testing and spinal cord atrophy at the corresponding metamere level was calculated.

Results

In the ventro-lateral aspect of the cervical cord, significant differences were detected in FA (p<0.0001), radial diffusivity (p<0.01) and MTR (p<0.01). No significant difference was detected in CSF-normalized T2-weighted (p=0.75) signal and axial diffusivity (p=0.72). The two-way ANOVA showed significant difference in spinal cord atrophy depending on the population (patient versus control, P=0.0002) and on the vertebral level (C4 to C7, P<0.0001). Pearson's coefficient showed a significant correlation between deltoid muscle testing and atrophy at the corresponding C5 metamere spinal level (p<0.01) and between muscle abductor pollicis brevis testing and atrophy at the corresponding C8 metamere spinal level (p<0.05).



Discussion.

Combining DW imaging and MT imaging is a promising approach to characterize spinal cord degeneration in ALS, as also been suggested in spinal cord injured patients [5]. We showed that spinal atrophy was correlated with some clinical measures. From a clinical perspective, it could provide new non-invasive tools for measuring disease progression in ALS.

References

1. Budde, M.D., et al., *Toward accurate diagnosis of white matter pathology using diffusion tensor imaging.* Magn Reson Med, 2007. **57**(4): p. 688-95.
2. Schmierer, K., et al., *Magnetization transfer ratio and myelin in postmortem multiple sclerosis brain.* Ann Neurol, 2004. **56**(3): p. 407-15.
3. Lundell, H., et al., *Independent spinal cord atrophy measures correlate to motor and sensory deficits in individuals with spinal cord injury.* Spinal Cord, 2010. **in press**.
4. Smith, S.M., et al., *Advances in functional and structural MR image analysis and implementation as FSL.* Neuroimage, 2004. **23 Suppl 1**: p. S208-19.
5. Cohen-Adad, J., et al., *Demyelination in the injured human spinal cord detected with diffusion and magnetization transfer imaging.* ISMRM, 2011.

Aknowledgments: François Salachas, Marie-Violaine Lebouteux, Timothée Lenglet, Stéphane Ouary and Olivier Freund. This study was supported by the Association Française contre les Myopathies (AFM) and by the Institut pour la Recherche sur la Moelle Epinière et l'Encéphale (IRME).