Quantitation of Corticospinal Tract Damage in Amyotropic Lateral Sclerosis Patients Using Diffusion Tensor Imaging

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Purpose

To utilize MR diffusion tensor imaging as a clinical tool to assess the fiber tract integrity of the posterior limb of internal capsule (PLIC) of amyotropic lateral sclerosis (ALS) patients. This study was also performed to evaluate the feasibility of using this technique as a new diagnostic tool in ALS.

Introduction

Amyotropic lateral sclerosis (ALS) is a progressive neuromuscular disease involving motor neurons. Degeneration of peripheral and central axons occurs in the white matter fiber tracts extending from the motor strip to the spinal cord (corticospinal tract). Most cases of ALS are sporadic and the cause is unknown. The rate of progression is variable. Currently, the diagnosis of this disease is one of exclusion requiring a careful clinical examination and series of diagnostic tests to rule out diseases that may mimic ALS. Considering that the life expectancy of an ALS patient is 2-5 years, it is important to develop a reliable non-invasive method, which can be used to diagnose the disease at an early stage that could allow for early therapeutic intervention (1-5).

Methods

Twelve patients with ALS and nine healthy volunteers were imaged using a clinical whole body MR scanner (1.5 T GE Signa Echospeed). In addition to clinical MR sequences (T_{1w}, T_{2w}, FLAIR) a diffusion tensor echo planar multislice imaging sequence was used. In order to cover the entire brain 30 axial slices with matrix of 128 by 128, FOV of 24 cm and slice thickness of 5mm were used. The diffusion-weighted images were collected in 7 non-collinear directions. The components of diffusion tensor (diffusion maps) were calculated. Using the tensor components an orientationally invariant diffusion constant ($D_{av} = \mathrm{Trace}\{\overline{\overline{D}}\}/3$) as well as an orientationally independent diffusion anisotropy map (UA_{surf}) was calculated for each pixel (6). UA_{surf} is dimensionless and its range is between 0 and 1.

The diffusion anisotropy of the PLIC was measured on each side by drawing 3 regions of interest on diffusion anisotropy maps; i) entire PLIC, ii) anterior 1/3 of PLIC, iii) posterior half of PLIC. The results from the right and left PLIC were averaged and then compared to the results from normal volunteers.

Results

The overall diffusion anisotropy of the PLIC of ALS patients was significantly decreased compared to normals (17%). In the anterior one-third of the PLIC, the anatomic location of the corticospinal tract, the decrease was more pronounced (28%) suggestive of selective white matter damage. This white matter damage was not apparent on routine MR sequences.

The tables below summarize our measurements. The inter-subject means and standard deviations are reported. In anisotropy measurements, the differences between patient group and the normals are all statistically significant ($p<0.05$). The average diffusion constant measurements (D_{av}), did not show any statistically significant difference between patient and normal group.

Diffusion Anisotropy (UA_{surf}) measurements of PLIC:

	Patients (n=12)	Normals (n=9)
entire PLIC	0.15±0.04	0.18±0.02
anterior 1/3 of PLIC	0.13±0.05	0.18±0.05
posterior 1/2 of PLIC	0.16±0.04	0.19±0.02

Average diffusion constant (D_{av}: $10^{-5}cm^2/s$) measurements of PLIC:

	Patients (n=12)	Normals (n=9)
entire PLIC	0.71±0.07	0.68±0.07
anterior 1/3 of PLIC	0.70±0.10	0.70±0.11
posterior 1/2 of PLIC	0.72±0.06	0.67±0.07

Discussion

The corticospinal tract (CST) is a major white matter fiber tract in the brain conveying information from the precentral gyrus (motor strip) to the spinal cord. There is strong restriction to water diffusion across this highly coherent fiber pathway. If a disease process, such as ALS, causes cellular damage to this particular fiber pathway, the coherence of the restriction that is normally imposed by the fiber over the water molecules will decrease. Therefore, it becomes possible to assess white matter fiber integrity by measuring its diffusion anisotropy.

We measured the diffusion anisotropy of the CST at the level of the basal ganglia in PLIC. We found statistically significant reduction of diffusion anisotropy in CST of ALS patients compared to healthy volunteers.

Routine MR imaging cannot reliably make the diagnosis of ALS. To exclude other diseases which mimic ALS, patients undergo a battery of diagnostic studies and a through neurologic examination. Since ALS patients have a markedly reduced life expectancy, the development of a reliable method to diagnose this disease at its earliest stages would be helpful to these patients, their families, and clinicians.

Conclusion

Diffusion tensor imaging can be performed as part of a routine brain MR and supplies reliable information concerning white matter fiber tract integrity that can not be obtained through standard MR imaging. We believe this information will be helpful in diagnosis of ALS and may prove useful in monitoring the progress of the disease.

References

1. Elliot J.L., Arch Neurol. 55, 911-912 (1998).
2. Pioro E.P., J. Neurol. Sci. 152, s49-53 (1997).
3. Block W. et al, Arch Neurol. 55, 931-936 (1997).
4. Chan S. et al, Radiology 212, 763-769 (1999).
5. Ulug A.M. et al, AJNR 20, 1044-1048 (1999).
6. Ulug A.M. & van Zijl P.C.M., JMRI 9, 804-813 (1999).