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Role of diffusion tensor imaging or magnetic resonance spectroscopy in the diagnosis and disability assessment of amyotrophic lateral sclerosis

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ABSTRACT

Objective: To compare the results of magnetic resonance spectroscopy (MRS) and diffusion tensor imaging (DTI) in amyotrophic lateral sclerosis (ALS) patients.
Methods: Nineteen ALS patients and thirteen age-matched healthy controls underwent MRS and DTI between October 2013 and July 2014. Fractional anisotropy (FA), apparent diffusion coefficient (ADC), N-acetylaspartate (NAA), choline (Cho), and creatine (Cr) were collected as the quantitative results of the imaging study. The ALS functional rating scale-revised (ALSFRS-R) and disease progression rate were evaluated to assess patients' disability. The imaging study results were compared between ALS patients and healthy controls. The relationship between disability assessment and imaging study results was analyzed.
Results: NAA/Cr in the motor cortex and FA in the corticospinal tract (CST) of both sides were significantly lower in patients than controls. There was no significant difference between the two groups in Cho/Cr, tract length, tract volume, ADC or NAA. No relationship was found between ALSFRS-R and FA ($r = 0.243$, $p = 0.316$) in the right CST; NAA ($r = 0.095$, $p = 0.699$) or NAA/Cr ($r = 0.172$, $p = 0.481$) in the left motor cortex; or NAA ($r = 0.320$, $p = 0.182$) or NAA/Cr ($r = 0.193$, $p = 0.492$) in the right motor cortex. There was no relationship between the disease progression rate and FA, NAA, or NAA/Cr on either side.
Conclusion: NAA/Cr and FA can help diagnose ALS. Regional brain NAA/Cr and FA values could not assess the ALSFRS-R or disease progression rate.

1. Introduction

Amyotrophic lateral sclerosis (ALS) is an idiopathic disorder of both upper and lower motor neurons, which displays a unique presentation of signs of upper and lower motor neuron degeneration in one or two limbs with predominantly cranial nerve or bulbar palsies. Unfortunately, ALS remains incredibly lethal and is resistant to a variety of therapies. We have not yet found a promising marker for diagnosing this disease in the early stage.

Conventional magnetic resonance imaging (MRI), which shows hypointensity in the motor cortex, brain atrophy and hyperintensity in the corticospinal tract (CST) [1], is only indicative of but not specific for ALS. FA measured on diffusion tensor imaging (DTI) examination displays more specific and significant changes in ALS.

Because progressive paralysis and the loss of life skills are two major aspects in the development of ALS, we have adopted the ALS functional rating scale-revised (ALSFRS-R) to monitor patients' disability and quality of life [2]. However, patients must lie quietly flat for 1 h when they are undergoing MRS and DTI; therefore, some patients with serious respiratory dysfunction should be excluded.

The diagnosis of ALS is still a challenging issue for most clinicians. Most patients are reluctant to see a doctor until late in the disease, and upper motor neuron (UMN) signs are easily ignored in physical examinations, especially when lower motor neuron (LMN) signs are typical. Moreover, the treatment currently remains difficult. Riluzole prolongs the lives of ALS patients but fails to stop the development of the disease. Epidemiological statistics reveal that approximately 50% of ALS patients survive more than 18 months after the diagnosis [1]. Therefore, it is imperative to find effective and objective markers for diagnosing ALS in the early stages and monitoring disease progression in follow-up [1].

We studied the ALS and healthy control groups by applying bilateral DTI of the CST and bilateral magnetic resonance spectroscopy(MRS) of the motor cortex to find a relatively simple and reliable method of diagnosing and assessing ALS disability.

2. Materials and methods

ALS patients and control individuals with right-handedness in Tongji Hospital were admitted to this study between October 2013 and July 2014. All ALS patients were diagnosed according to the Revised El

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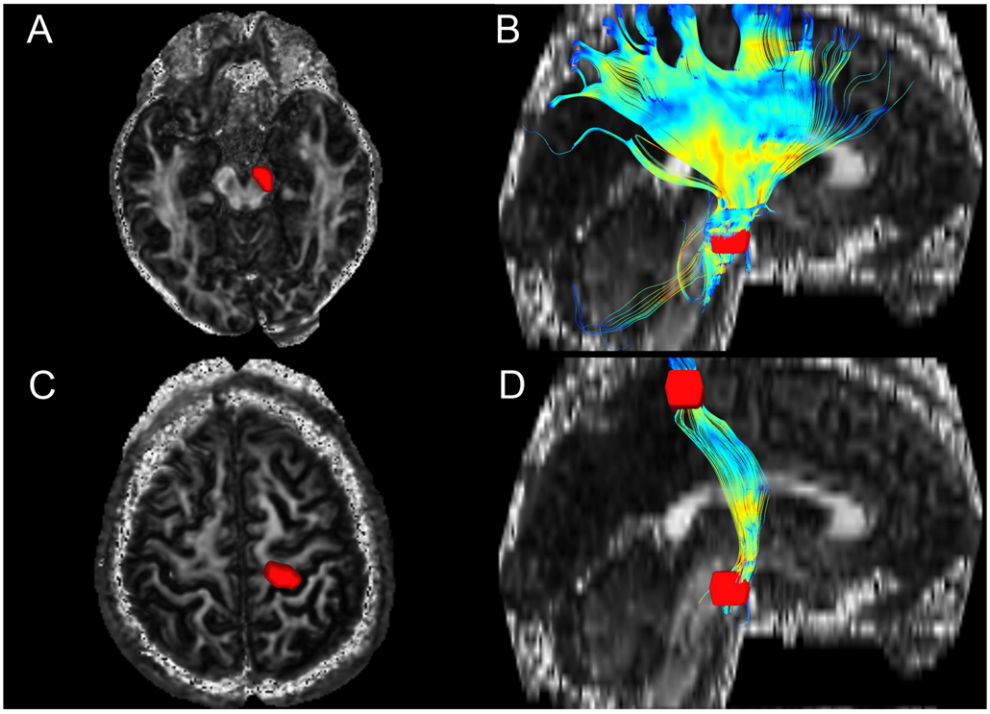

Fig. 1. Fiber tracking of left CST. A seed region was first positioned in the left cerebral peduncle. According to the tracking fibers, another region was properly placed in the left precentral gyrus, and the left CST was obtained.

Escorial criteria. ALS patients who could not lie flat for 1 h or needed ventilation or who suffered from Hirayama syndrome, Kennedy's disease, paraneoplastic syndrome, multifocal motor neuropathy, primary lateral sclerosis or monomelic amyotrophy were excluded. Each patient's medical record was retrospectively reviewed. All patients consented to provide information for the investigation, and the study was approved by the Clinical Institute Ethics Committee.

ALSFRS-R and the disease progression rate (based on the formula 48-ALSFRS-R / months of disease duration) were used to evaluate and monitor disability in each ALS patient.

Thirteen age-matched healthy controls with no history of neurological or psychiatric diseases agreed to be recruited for the study. Additionally, if any abnormalities on T1-weighted or T2-weighted MRI were detected, the patient was excluded from the control group.

Nineteen ALS patients were included and underwent evaluation using the ALSFRS-R and the disease progression rate.

2.1. Routine MR imaging

All subjects underwent an MR scan on a 3.0-T MR scanner (GE Discovery LS MR 750) with a 32-channel head coil. Routine MRI sequences included axial T2-FLAIR (TR, 8000 ms; TE, 160 ms; TI, 2100 ms; NEX, 1; matrix, 256 × 256; FOV, 240 × 240 cm^2; section thickness, 5 mm; and spacing, 1.5 mm) and axial 3D T1-BRAVO (TR, 8.2 ms; TE, 3.2 ms; prep time, 450 ms; NEX, 1; matrix, 256 × 256; FOV, 240 × 240 cm^2; and section thickness, 1.2 mm). Sagittal and coronal images reformatted from axial 3D T1-BRAVO and axial images were used to position the spectroscopic voxels. The scan plane parallel to the line combined the

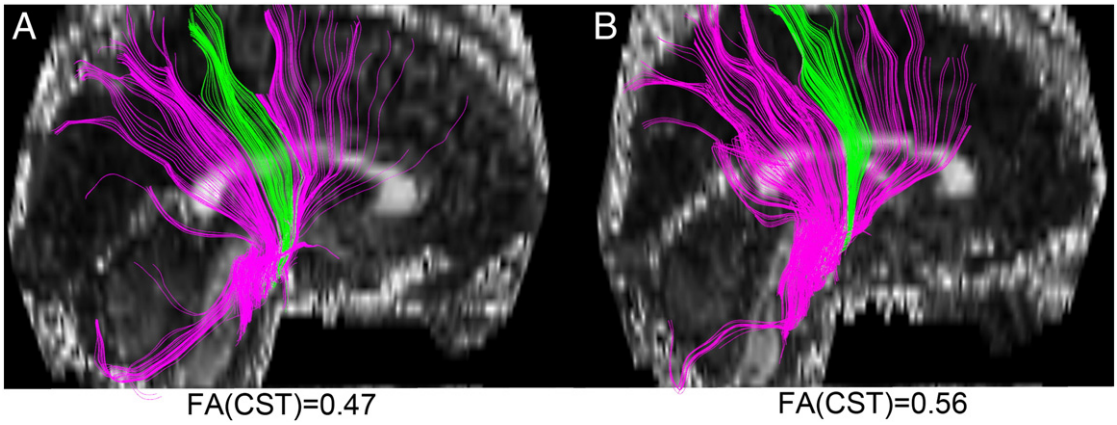

Fig. 2. Fiber tracking images of an ALS patient (A) and an age-matched healthy control (B). Fibers connecting the cortex and brain stem are shown in purple. The right CSTs are shown in green. The FA of the right CST fiber was diminished in the ALS patients (A) compared with the control subjects (B).