A Longitudinal Study of Diffusion Tensor Imaging (DTI) in ALS

C. R. Blain[1], V. C. Williams[1], M. R. Turner[1], C. Smallman[1], S. Landau[2], D. K. Jones[1], G. J. Barker[1], S. C. Williams[1], P. N. Leigh[1], A. Simmons[1]
[1]Neurology, Institute of Psychiatry, London, United Kingdom, [2]Biostatistics, Institute of Psychiatry, London, United Kingdom

Objective

To use Diffusion Tensor Imaging (DTI) to measure progression of damage within the corticospinal tract in Amyotrophic Lateral Sclerosis (ALS).

Background

Upper motor neuron (UMN) damage is difficult to assess clinically in ALS due to masking by lower motor neuron (LMN) signs. DTI detects damage in the corticospinal tracts of patients with ALS and could provide an objective biomarker of UMN disease progression.

Methods

21 ALS subjects and 24 healthy volunteers were recruited into a longitudinal study. Clinical severity was measured in the ALS patients using the ALSS and ALSFRS-R. Each subject underwent DTI at the first time point and was invited to return for a second scan six months later. At both time points, whole brain optimised DTI data (1) were acquired using a 1.5 Tesla General Electric NV/*i* MR system using a conventional birdcage head coil. Following correction for eddy-current distortion Mean Diffusivity (MD) and Fractional Anisotropy (FA) measurements with an isotropic resolution of 2.5mm were computed for each voxel using in-house software. Regions of interest within the corticospinal tract (motor cortex, subcortical white matter, internal capsule and cerebral peduncle) were selected from the T2 weighted (b=0) images and transposed onto inherently co-registered MD and FA maps. For both FA and MD, repeated measures multivariate ANOVA was used to test for effects of group and region and their interactions with time.

Results

10 ALS subjects and 11 controls underwent both scans. There was a trend towards functional deterioration as measured by ALSS (paired t-test, p=0.068) and ALSFRS-R (paired t-test, p=0.05). For both FA (F=10.1, df(1,19), p=0.005) and MD (F=9.73, df(1,19), p=0.006) within the corticospinal tract, the ALS group were different to controls. However, there was no interaction between group and time for either FA (Hotelling's trace: F=0.63, df(1,19), p=0.44) or MD(Hotelling's trace test: F=0.44, df(1,19), p=0.513).

Conclusions

DTI was able to detect damage within the corticospinal tract in the small group of ALS patients able to undergo scans at both time points, but could not detect statistically significant change over this short time period. This result highlights the difficulties inherent in a longitudinal MRI study of patients with a rapidly progressive disease such as ALS, where a negative result could represent a lack of statistical power.

Study Support

MND Association of Great Britain and Northern Ireland

References

1. Jones et al. (2002) Hum Brain Mapp 15:216-230