Corticospinal Tract Damage in Patients Homozygous for the D90A SOD1 Gene Mutation Compared to Sporadic ALS : A Diffusion Tensor Imaging Study

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Objective

To use diffusion tensor imaging (DTI) to identify structural changes in the corticospinal tract (CST) in patients with sporadic ALS (sALS) compared to familial ALS patients with homozygous D90A SOD1 mutations (homD90A).

Background

Patients with homD90A show a stereotyped phenotype comprising an ascending spastic paraparesis, with development of lower motor neuron and bulbar signs over 10 to 20 years. The phenotype in sALS patients is much more variable. Recent electrophysiological and functional imaging studies suggest differences in the pattern of cortical neuronal vulnerability between homD90A and sALS cases. These findings, together with the clinical phenotype, suggest that homD90A cases may have a predominantly dying back CST pathology, compared to sALS. DTI provides a technique to examine CST pathology *in vivo.*

Methods

Seven homD90A and 21 sALS subjects were compared to 18 healthy age-matched controls. For each subject 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. To avoid bias, 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. These regions were transposed on to inherently co-registered MD and FA maps and their values extracted. For both FA and MD, repeated measures multivariate ANOVA was used to test for effects of group, region and their interaction and appropriate *post hoc* tests performed.

Results

For both FA ($F=3.97$, df(2,43), $p=0.026$) and MD ($F=6.46$, df(2,43), $p=0.004$), there was a significant effect of group alone. *Post hoc* tests revealed that MD was significantly increased in the corticospinal tract in both the homD90A group ($p=0.002$) and sALS ($p=0.011$) groups compared to controls, with a trend to reduction in FA in the homD90A group ($p=0.121$) and significant reduction in FA in sALS ($p=0.008$). There were no significant differences in MD or FA in the corticospinal tract between the homD90A and sALS groups.

Conclusions

This study confirms that DTI is able to detect damage to the intracranial CST in ALS subjects. The similar degree of CST involvement in both the homD90A and sALS patients suggests that degeneration in the CSTs is similar in the two groups despite the differences in phenotype. These findings do not support our hypothesis that the distribution of CST degeneration differs in sALS compared to homD90A.

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References

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