Diffusion tensor imaging in sporadic and familial (D90A SOD1) forms of amyotrophic lateral sclerosis

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Background

Amyotrophic Lateral Sclerosis (ALS) is a devastating neurodegenerative disorder, which principally targets the motor system. Diffusion tensor imaging can be used to visualise degeneration of the corticospinal tract and extra-motor regions in ALS patients(1). In contrast to the variable phenotype of sporadic ALS (sALS), familial ALS patients homozygous for the D90A SOD1 mutation (homD90A) show a stereotyped phenotype of slowly ascending spastic paraparesis. Electrophysiological and PET imaging studies have suggested differences in the pattern of cortical neuronal vulnerability between homD90A and sporadic ALS cases(2). We used diffusion tensor imaging to test the hypothesis that homD90A patients show less extensive white matter pathology than that seen in sALS.

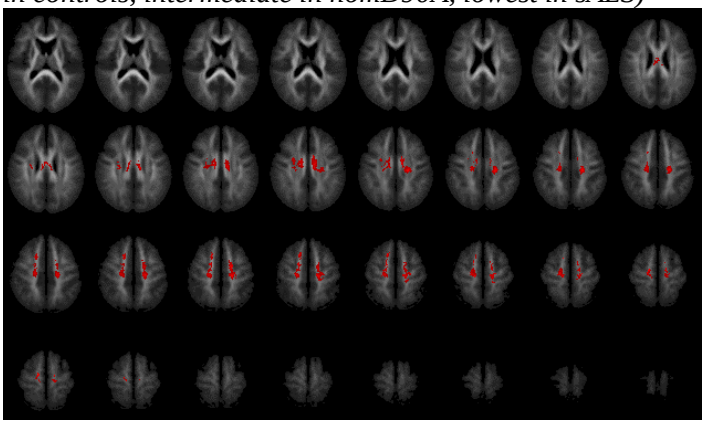
Methods

Six homD90A patients, 20 sALS patients and 21 control subjects underwent axial whole brain DTI using a 1.5T GE Signa LX NV/i system. An optimised DTI acquisition scheme with isotropic (2.5mm) voxels was used (TE=107ms, effective TR=15 R-R intervals, duration of diffusion-encoding gradients=17.3ms, maximum diffusion weighting of 1300 s mm-2). Following calculation of the diffusion tensor, maps of mean diffusivity (MD) and fractional anisotropy (FA), two indirect indices of microstructural integrity, were constructed. Images were transformed to Talairach space, smoothed and the WM masked from the rest of the brain. A voxel-based analysis technique was used to perform a three-way ANOVA testing the hypothesis of a linear trend in MD and FA between controls, homD90A and sALS cases. A confirmatory 2-way ANOVA comparing the two disease groups was also performed. Within the ALS group, correlations between white matter indices and clinical measures (ALSFRS-R and UMN scores) were examined.

Results

Disease severity assessed by ALSFRS-R scores was similar in the sALS and homD90A patients (sALS mean =37.75, SD 7.3; homD90A mean = 36.17, SD 6.2). Disease duration was longer in the homD90A patients (sALS mean 28.4 months, SD18.4; homD90A mean 46.3, SD 50.0). The three-way ANOVA confirmed our hypothesis of a linear trend in FA (controls>HomD90A>ALS; Figure 1) and MD (controls<HomD90A<ALS) in the corona radiata and the corpus callosum (particularly in the region linking the pericentral gyri). MD also showed this pattern in the cerebral peduncles and in some extra-motor pathways, including the temporal stem and occipitotemporal fibres. The two way ANOVA confirmed that changes in both FA and MD in these regions were more marked in sALS compared with D90A ALS cases. In the sALS group, ALSFRS-R and UMN scores were correlated with the extent of white matter damage in motor pathways assessed by both FA and MD.

Figure 1: Map of voxels with a linear trend in FA (highest in controls, intermediate in homD90A, lowest in sALS)



Discussion

These results confirm previous reports of reduced FA and increased MD in the corticospinal tracts and extra-motor pathways in ALS. We have confirmed that changes in FA and MD are correlated with disease severity, and shown for the first time a relationship with the extent of upper motor neuron damage assessed clinically. Despite similar disease severity and longer disease duration in the homD90A group, degeneration of motor and extra-motor pathways is less marked in this form of familial ALS compared to sALS cases. This supports the notion that genotype influences the pathological phenotype in ALS and that DTI may provide a useful *in vivo* method of investigating cellular mechanisms of neurodegeneration across phenotype and genotype.

References

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