

Modelling the trajectory of cortical atrophy in Huntington's disease
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Background

Despite histological evidence of widespread grey matter atrophy by end-stage Huntington's disease (HD), the progression of cortical atrophy in HD has yet to be fully characterised.

Aims

Here, we aim to map cortical atrophy during the transition from premanifest to motor clinical diagnosis of manifest HD, modelling both non-linear and linear atrophy rates in a large cohort of participants, with MRI data spanning 6 years before and 5 years after clinical diagnosis.

Methods

Structural MR images from 49 HD gene-carrier participants were included in the analysis, collected as part of the longitudinal, multi-site TRACK-HD and TrackOn-HD studies. Participants underwent yearly 3T MRI scans, with some participants returning for 7 visits, and were classified as premanifest at recruitment with diagnosis as manifest HD occurring at a later time-point. Each set of images for each participant underwent longitudinal registration and were segmented using MALP-EM, with cortical and subcortical volumes calculated. A hierarchical dynamical model was applied at the individual level to map individual trajectories. A group level model was then used to estimate group-wise change, accounting for covariates. This approach was used to measure gross atrophy, linear rate of atrophy and non-linear accelerations in atrophy.

Results

Atrophy was highest in frontal and motor regions, particularly the supplementary motor cortex (11.66% per decade) with greatest linear rates of atrophy in the frontal cortex and greatest acceleration of atrophy in the motor cortex.

Conclusions

This study provides the most complete characterisation of cortical atrophy in HD presented to-date. The results suggest that the amount of atrophy occurring in the cortex around time of HD

diagnosis is much higher than previously reported, and a number of regions show accelerations in atrophy. These findings have important implications for the understanding and treatment of HD and other neurodegenerative conditions.