Biological and Clinical Characteristics of Gene Carriers Far From Predicted Onset in the HD Young Adult Study: A Cross-Sectional Analysis

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AIM: TO IDENTIFY THE EARLIEST HD CHANGES AND ROBUST OUTCOME MEASURES FOR CLINICAL TRIALS

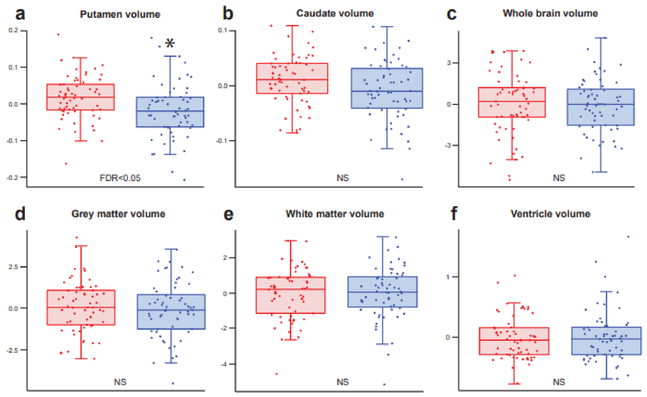
BACKGROUND

- Disease-modifying treatments are in development for HD
- Intervention at the start of the neurodegenerative process whilst clinical function still intact may delay or prevent onset

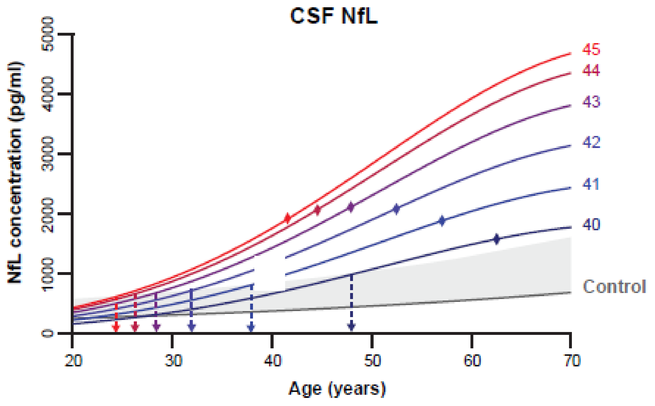
METHODS

67 controls and 64 preHD approx. 24 years from expected onset underwent clinical, cognitive, neuropsychiatric, imaging and biofluid assessments

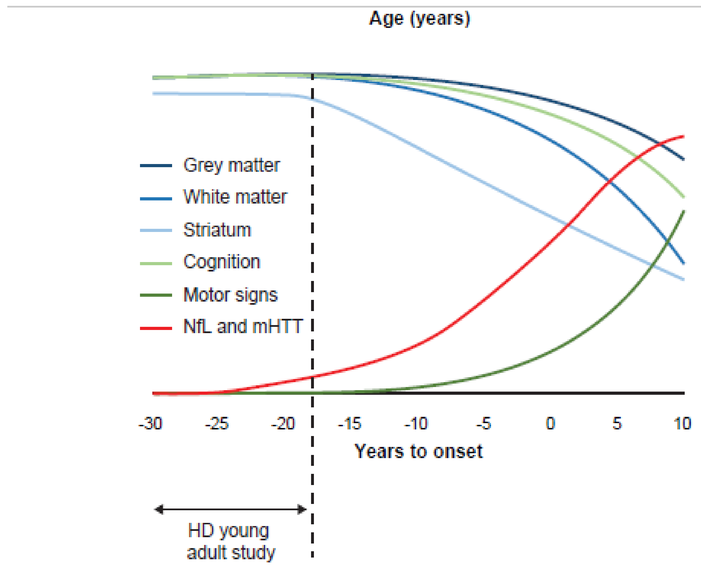
RESULTS



Significantly reduced putamen volumes (q=0.03) in preHD. No other brain metrics survived FDR correction (q>0.16); no association with disease burden (q>0.48)



CSF and plasma NfL(q<0.0001 and q=0.01) and YKL-40 (q=0.03) elevated in preHD; elevations more likely in those closer to onset



No significant cognitive or neuropsychiatric impairment > 20 years from onset

CONCLUSIONS

Elevated NfL suggests early neuronal damage up to 24 years prior to symptom onset in the absence of functional impairment

Reduced putamenal volumes may represent the start of neurodegeneration or may reflect different neurodevelopmental processes in gene carriers

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