Identification of genetic variants associated with Huntington’s disease progression: a genome-wide association study

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24 quantitative motor, cognitive & imaging variables from TRACK-HD with tractable metric properties: annual data over 3y (Supp. Table 2)

Control for age, CAG repeat length, site, gender, education; & their interactions with follow-up time

Calculate each subject’s residual random longitudinal slope from a mixed effect regression model

Principal component analysis of the residual random slopes

Use 1st Principal Component as the TRACK-HD progression score: based on longitudinal change over 3y

TRACK-HD unified Huntington's disease progression measure (N=218)

Genotype & quality control

Genome wide association analysis in terms of progression (N=216)

REGISTRY unified Huntington's disease progression measure (N=1835)

Obtain genetic data from GeM-HD

Genome wide association analysis in terms of progression (N=1773)

Data integration:
1. Correlation between onset and progression in (i) TRACK-HD and (ii) REGISTRY;
2. Correlation of unified HD progression measures between TRACK-HD and REGISTRY;
3. Meta-analysis of unified HD progression association in TRACK-HD and REGISTRY;
4. Pathway, expression, STRING analyses.
Symptoms / signs of HD

Age at onset

- REGISTRY
  - atypical severity measure:
  - Cross sectional progression to time D
- TRACK HD
  - progression measure:
  - Progression over 3 years between time A and C
- AAO
  - progression to time B in the motor domain

Time (years): the letters A, B, C, D indicate points in time

Histograms:
- TRACK-HD Atypical Progression PC scores (SD)
- Registry Atypical Residual Severity Scores