Defining Clinical Progression of Juvenile-Onset Huntington's Disease:

An Enroll-HD Analysis

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Background: Patients with Juvenile-Onset (JOHD) have a unique, hypokinetic presentation compared to patients with adult-onset HD (AOHD) who present with hyperkinetic symptoms. Patients with AOHD sometimes experience hypokinetic symptoms in the late stages of the disease. Therefore, it is unclear if the unique phenotype seen in JOHD is caused by novel pathologic mechanisms or if these patients reach a hypokinetic stage much earlier in the disease. We leveraged the Enroll-HD database to compare motor patterns of JOHD to patients with AOHD and early-onset HD (EOHD).

Methods: Patients with HD were splint into those with JOHD (CAG >60 and age of motor onset (AMO) ≤ 21 years), EOHD (CAG >45 and AMO between 21 and 30), or AOHD (CAG ≤ 45 and AMO >30). We used non-linear mixed effect regression models to compare the trajectory of the total motor score (TMS) between groups controlling for age, CAG, sex, and medications that affect motor presentation. Similar models were constructed to compare trajectories for all subscales of the UHDRS across groups.

Results: TMS progression was fastest in the JOHD group, followed by the EOHD and AOHD groups. However, chorea decreased over time in the JOHD group while hypokinetic symptoms increased at a significantly faster rate compared to the EOHD and AOHD groups.

Conclusion: The unique motor symptoms in JOHD most likely are not the result of novel neuropathologic mechanisms; rather, they likely represent the accelerated trajectory of motor symptoms that start hyperkinetic and then progress to hypokinetic.