Abstract

Background: The cohort-level risk of Huntington disease (HD) is related to the age and symptom level of the cohort, but this relationship has not been made precise.

Objective: To predict the evolving likelihood of carrying the Huntington disease (HD) gene for at-risk adults using age and sign level.

Methods: Using data from adults with early signs and symptoms of HD linked to information on genetic status, we use Bayes' theorem to calculate the probability that an undiagnosed individual of a certain age and sign level has an expanded CAG repeat.

Results: Both age and sign levels have substantial influence on the likelihood of HD onset, and the probability of eventual diagnosis changes as those at risk age and exhibit (or fail to exhibit) symptoms. For example, our data suggest that in a cohort of individuals age 26 with a Unified Huntington's Disease Rating Scale (UHDRS) motor score of 7-10 70% of them will carry the HD mutation. For individuals age 56, the same motor score suggests only a 40% chance of carrying the mutation. Early motor signs of HD, overall and the chorea subscore, were highly predictive of disease onset at any age. However, body mass index (BMI) and cognitive performance scores were not as highly predictive.

Conclusions: These results suggest that if researchers or clinicians are looking for early clues of HD, it may be more foretelling to look at motor rather than cognitive signs. Application of similar approaches could be used with other adult-onset genetic conditions.

Keywords: Huntington disease (HD); bayesian; diagnosis; early symptoms; predictive.