ANTICIPATION IN E200K CREUTZFELDT-JAKOB DISEASE PATIENTS OF THE CALABRIAN CLUSTER: AN OBSERVATIONAL STUDY

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Introduction: The term anticipation in genetic disease refers to earlier age at onset and/or increased severity in successive generations. Anticipation has been shown in several neurodegenerative diseases such as Huntington’s disease, spinocerebellar ataxia type 1, and myotonic dystrophy, where the gene linked to the disease is affected by trinucleotide repeat instability, with expansion of repeats clearly correlated with an earlier age at onset. Preliminary evidence has shown anticipation in genetic Creutzfeldt-Jakob disease (CJD) linked to the E200K mutation among Libyan Jews.

Aims: The aim of the present study was to investigate whether genetic anticipation may occur among E200K CJD patients of the Calabrian cluster.

Methods: We recorded the age at death of 31 parent-offspring pairs from 19 pedigrees. Age at death was given as mean, and range. The paired t-test was performed to test the statistical significance of paired differences.

Results: The mean age at onset was 59.2 (39-87) in CJD offspring and 71.7 years (50-91) in the parent generation. The difference in the mean age at diagnosis between parents and their offspring was 11.7 years (95% confidence interval 6.2-17.2), and statistically significant (p< 0.0001).

Conclusion: These results suggest that anticipation is present in the Calabrian cluster of E200K CJD cases. Although we cannot completely exclude ascertainment biases, the study design was intended to minimize them. Further studies on large multigenerational and systematically recorded pedigrees are needed to confirm the data. The basis for the anticipation in genetic E200K CJD is unknown.