Supplemental data

*Figure e-1: Flow chart of patients who met inclusion/exclusion criteria for the study, excluding non-C9orf72 repeat expansion gene mutations carriers*.

*(A) All ALS patients registered with Irish ALS Register from 1994 through 2016 who reported a history of suspected or confirmed ALS or FTD in at least one relative were identified. All patients with an ALS causative gene (C9orf72 repeat expansion) were identified from the DNA database. (B). 35 patients* *with a family history suspicious for ALS or FTD in whom it was not possible to confirm the relatives’ diagnoses and 9 patients with Kennedy’s disease were excluded. 6 C9orf7- positive patients with a family history suspicious for ALS or FTD in whom it was not possible to confirm the relatives’ diagnoses were recategorized as “gene-isolated-FALS”.*

*C9orf72* negative

B

A

30

1022

48

138

59

219

2173

DNA bank

ALS register

14

Exclude 5 6

Exclude 44 44Exclude 44

4

ALS and FTD

ALS

FTD

35

*C9orf72* positive only

Confirmed positive family history

*C9orf72* positive

Family history positive only

*C9orf72* positive and family history positive

*C9orf72* positive only

23

12

38

*Figure e-2: Family histories of C9orf72-positive patients who did not meet Byrne criteria for FALS.*

|  |  |
| --- | --- |
| No. |  |
| 1 | No information available on family. |
| 2 | No information available on second-degree relatives. |
| 3 | 2 first-degree relatives had dementia |
| 4 | No information available on second-degree relatives. |
| 5 | No information available on second-degree relatives. |
| 6 | 1 first-degree relative and 1 second-degree relative committed suicide. |
| 7 | No information available on family. |
| 8 | 1 first-degree relative had dementia and 1 third-degree relative had multiple sclerosis |
| 9 | No information available on family. |
| 10 | 1 first-degree relative had Parkinson’s Disease. 1 second-degree relative had Parkinson’s Disease. 1 second-degree relative had dementia. |
| 11 | No information available on paternal side of family. 1 second-degree relative committed suicide. |
| 12 | 1 first-degree relative and 1 second-degree relative had schizophrenia. |
| 13 | 4 out of 6 siblings died under the age of 40. Incomplete information available on second-degree relatives. |
| 14 | 3 second-degree relatives had Alzheimer’s dementia. |
| 15 | 1 first-degree relative had dementia. |
| 16 | 1 second-degree relative had dementia. |
| 17 | 3 first-degree relatives had dementia and 1 second-degree relative had autism. |
| 18 | 1 first-degree relative had schizophrenia. 1 second-degree relative had schizophrenia. 2 third-degree relatives committed suicide. 1 second-degree relative had neuropsychiatric disorder (unspecified). |
| 19 | 2 first-degree relatives with Bipolar affective disorder, one of whom committed suicide. |
| 20 | 3 second-degree relatives with neuropsychiatric disorders (unspecified). |
| 21 | 1 first-degree relative had alcohol dependence disorder. |
| 22 | 1 first-degree relative and 1 second-degree relative had Alzheimer’s dementia. 2 second-degree relatives had Parkinson’s Disease. 1 second-degree relative and 4 third-degree relatives had alcohol dependence disorder. |
| 23 | 4 first-degree relatives had alcohol dependence disorder. |
| 24 | 1 first-degree relative had dementia. |
| 25 | 2 second-degree relatives had neuropsychiatric disorders (unspecified). |
| 26 | 1 second-degree relative had Alzheimer’s dementia. |
| 27 | 1 first-degree relative had schizophrenia. 1 first-degree relative had bipolar affective disorder. 1 second-degree relative had alcohol dependence disorder. |
| 28 | 1 first-degree relative had dementia. 2 first-degree relatives had alcohol dependence disorder. 1 second-degree relative had neuropsychiatric disorder (unspecified). 1 second-degree relative had multiple sclerosis. |
| 29 | 1 first-degree relative and 2 second-degree relatives had Alzheimer’s dementia. |
| 30 | 1 first-degree relative dementia |
| 31 | 1 first-degree relative had schizophrenia and alcohol dependence disorder. Suspect 1 second-degree relative had ALS. |
| 32 | 1 first-degree relative and 3 second-degree relatives had dementia. 1 third-degree relative had Parkinson’s Disease. Suspect 1 second-degree relative had ALS. |
| 33 | 1 second-degree relative had dementia. Suspect first-degree relative had ALS. |
| 34 | Suspect first-degree relative had ALS. |
| 35 | 1 first-degree relative had Bipolar affective disorder. Suspect first-degree relative had ALS-FTD and second-degree relative had ALS. |