Symptom Onset in Genetic Frontotemporal Dementia

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on behalf of the Frontotemporal dementia Prevention Initiative (FPI)

Background

Genetic frontotemporal dementia (FTD) is caused by mutations in three main genes: *C9orf72*, progranulin (*GRN*) and microtubule-associated protein tau (*MAPT*). Little is currently known about the factors that influence age at symptom onset in FTD. This study aimed to investigate this through data collected from multiple families through the Frontotemporal dementia Prevention Initiative (FPI), a group connecting research centres within four large studies: GENFI, ARTFL, LEFFTDS and DINAD.

Materials and Methods

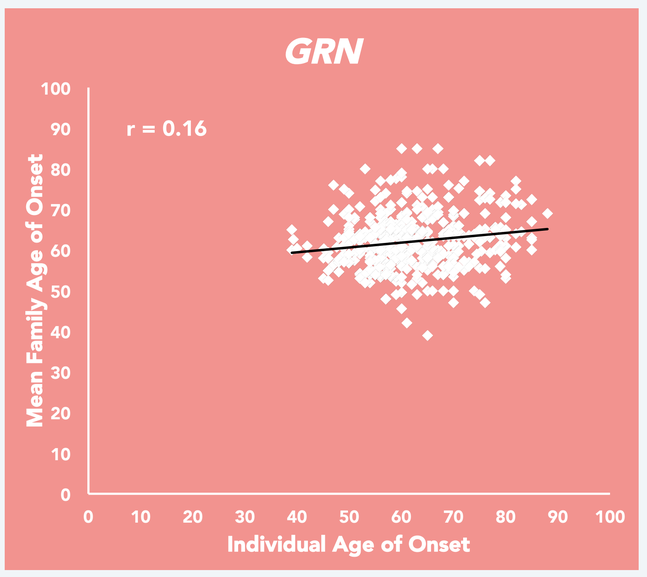
We have so far collected data on ages at symptom onset from 2192 individuals from 915 families seen at 34 centres across the world: 854 *C9orf72* (426 families), 504 *MAPT* (152 families: 60 different mutations, most common P301L), and 834 *GRN* (337 families: 101 different mutations, most common T272fs).

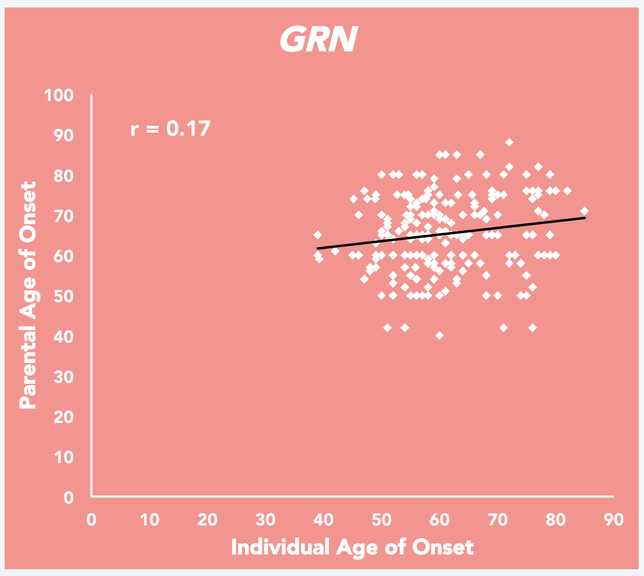
Results

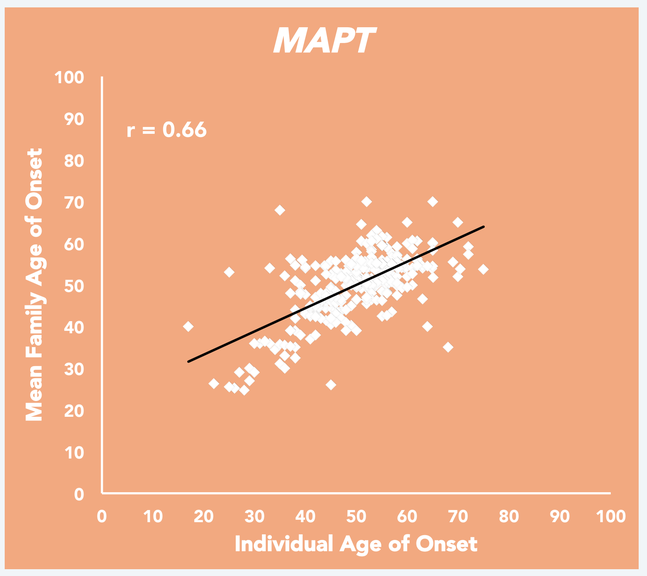
The mean age at onset (AAO) was 58.4 (standard deviation 10.7) in *C9orf72*, 49.9 (9.9) in *MAPT*, and 61.3 (9.3) in *GRN*. In a preliminary analysis we investigated the correlation of AAO with parental AAO and mean AAO within the family. The strongest correlation between individual AAO and both parental AAO (r = 0.55, p<0.001) and mean AAO in the family (r = 0.66, p <0.001) was seen in *MAPT*, with a higher correlation with mean AAO in the family. In *C9orf72*, there was also a significant correlation between individual AAO and both parental AAO (r = 0.33, p=0.001) and mean AAO in the family (r = 0.31, p <0.001) but to a lesser extent than *MAPT*. The lowest correlation of individual AAO with parental age at onset (r = 0.17, p<0.05) and mean AAO in the family (r=0.16, p<0.001) was in *GRN* although these were nonetheless both still significant.

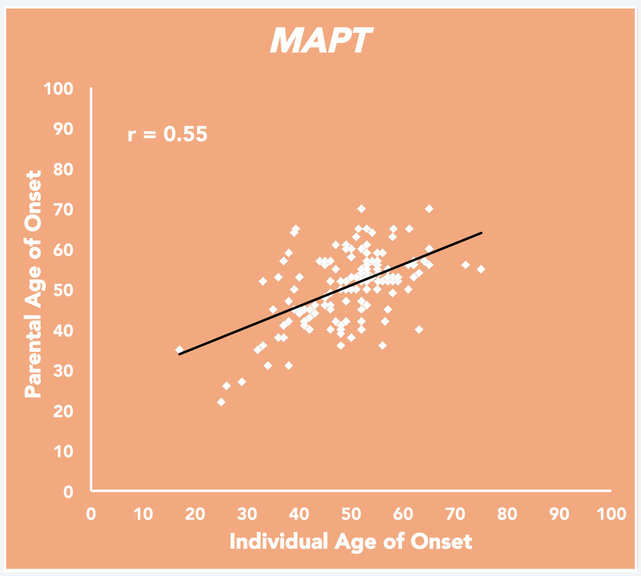
Conclusion

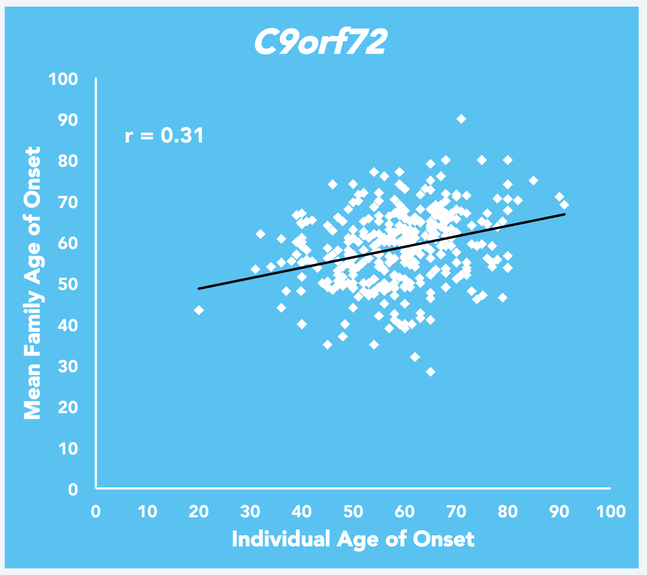
Whilst a proportion of the observed variance in age at symptom onset in genetic FTD can be explained by family history this is variable by mutation type.

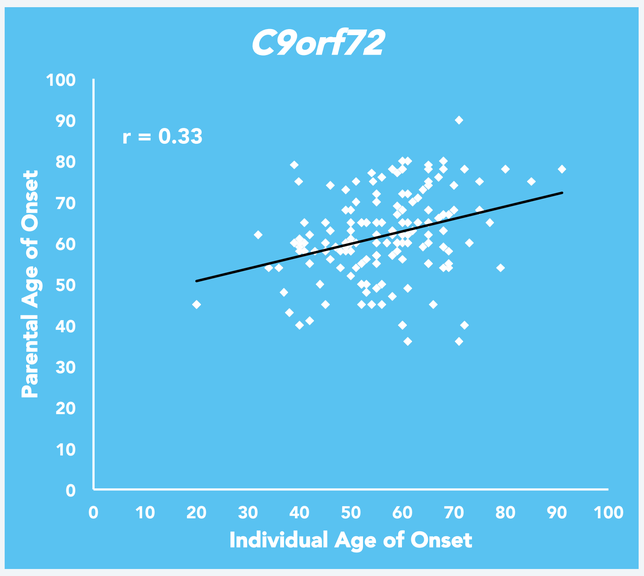






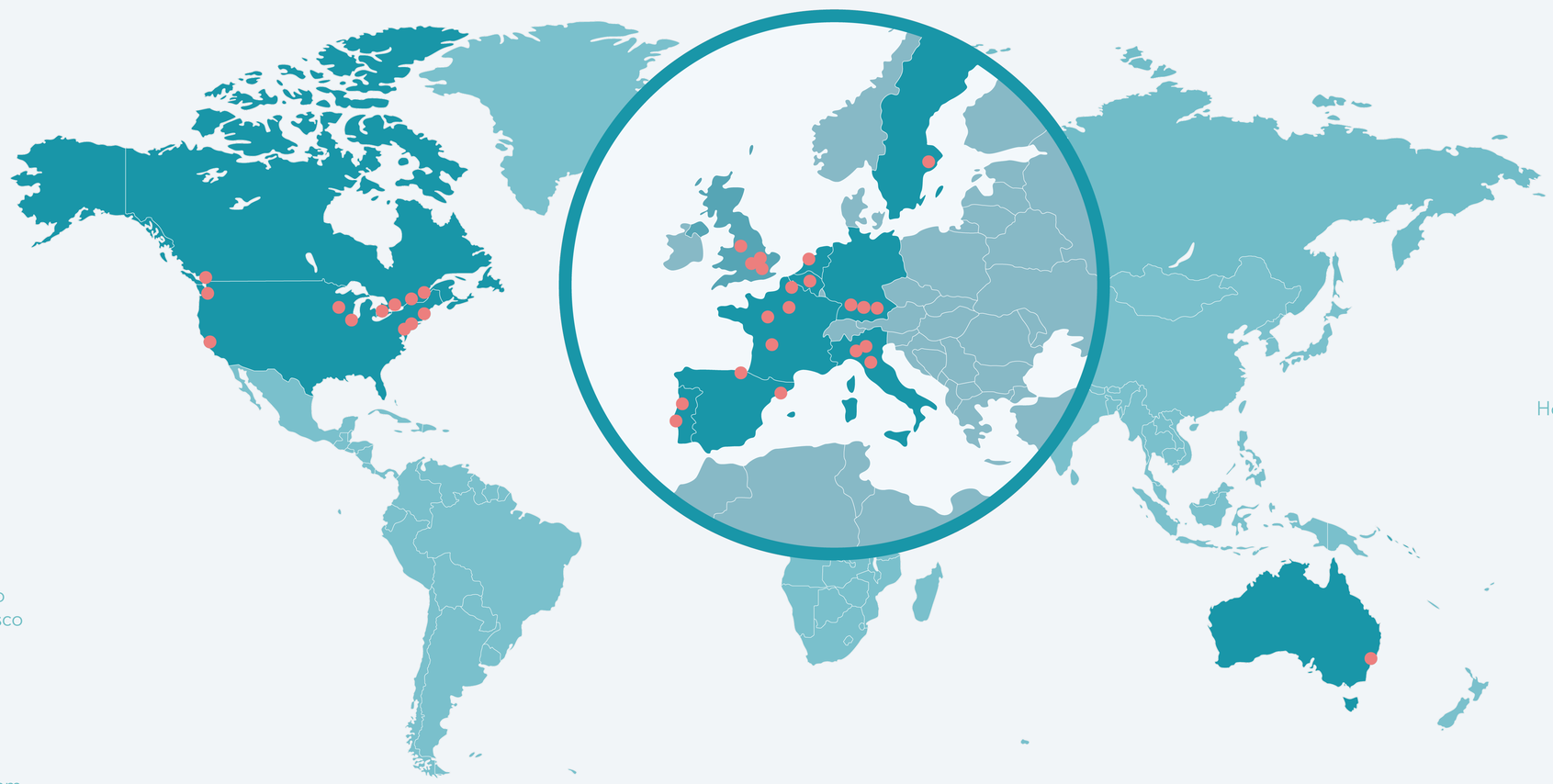






Figures 1-3: Scatter plots showing the relationship between individual age of onset and mean family age of onset in the three mutation groups

Figures 4-6: Scatter plots showing the relationship between individual age of onset and parental age of onset in the three mutation groups



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Longitudinal Evaluation of Familial FrontoTemporal Dementia Subjects LEFFTDS

DNAD Dominantly Inherited Non-Alzheimer Dementias

FPI FTD Prevention Initiative

KMD is supported by an Alzheimer's Society PhD Studentship. JDR is an MRC Clinician Scientist and has received funding from the NIHR Rare Diseases Translational Research Collaboration. See individual study websites for details of funding for the GENFI, LEFFTDS, ARTFL and DINAD centres. Author affiliations and a complete author list for the FPI are available on request from j.rohrer@ucl.ac.uk.