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Ventricular volume expansion in presymptomatic genetic frontotemporal dementia

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Study objective and summary result

This study aimed to characterize the timecourse of ventricular volume expansion in persons carrying genetic mutations associated with frontotemporal dementia (FTD), and found that ventricular volume expansion is greater in presymptomatic mutation-carriers than in noncarriers who are biologically related to symptomatic mutation-carriers.

What is known and what this paper adds

Ventricular expansion is a consistently observed feature of genetic FTD at the symptomatic stage. This investigation shows that it can also be observed during presymptomatic stages.

Participants and setting

This investigation included 46 presymptomatic carriers of FTD-associated mutations in *MAPT*, *PGRN*, or *C9orf72* and 56 noncarriers. These participants were all first-degree relatives of symptomatic mutation carriers. These individuals participated in the Genetic FTD Initiative (GENFI), which recruited participants through 12 sites in Canada, Sweden, Italy, the UK, and the Netherlands.

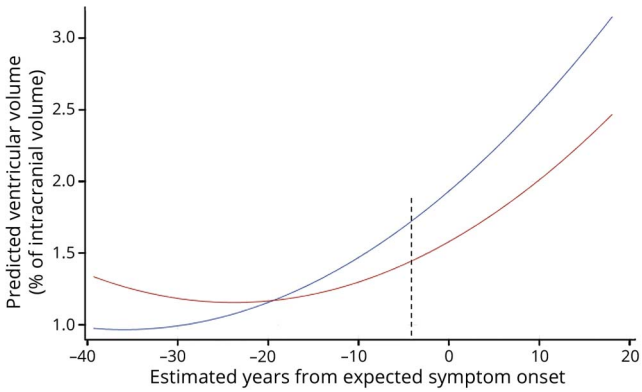
Design, size, and duration

The participants underwent baseline and 1-year follow-up assessments that included volumetric T1-weighted MRI scans. Total ventricular volumes were calculated by summating the volumes of the left and right lateral ventricles, the third ventricle, and the fourth ventricle, and they were expressed as percentages of total intracranial volumes. Linear mixed models were used for between-group comparisons of ventricular expansion timecourses. For each participant, an expected age at symptom onset was calculated as the difference between the participant's age and the mean age at symptom onset within the participant's family.

Main results and the role of chance

Relative to the noncarriers, the presymptomatic carriers had greater annualized rates of ventricular expansion (model estimate ± standard error, 0.35 ± 0.15; $p = 0.02$). Between-group differences in ventricular volumes were observed 4 years before the expected ages at symptom onset ($p = 0.04$).

Figure Total ventricular volumes plotted against years from expected symptom onset in the presymptomatic carriers (blue) and the noncarriers (red)



The dashed black line indicates the point at which between-group differences arose.

Bias, confounding, and other reasons for caution

This investigation's sample size was limited for some subgroup analyses. This investigation relied on predicted ages at onset instead of observed ages at onset.

Generalizability to other populations

This investigation's reliance on data from high-income Western countries may limit the generalizability of the results.

Study funding/potential competing interests

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