

Temporal dynamics predict symptom onset and cognitive decline in familial frontotemporal dementia

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State of the art

Functional network integrity is important for maintaining cognitive performance in individuals at risk of dementia. We investigated whether changes in functional networks predict cognitive decline and conversion from the presymptomatic prodrome to symptomatic disease in familial frontotemporal dementia (FTD).

Methodology

For hypothesis generation, 36 participants with behavioural variant FTD and 34 healthy controls were recruited from the Cambridge University Centre for Frontotemporal Dementia. For testing of the derived pre-registered hypotheses, 198 symptomatic FTD mutation carriers, 341 presymptomatic mutation carriers and 329 family members without mutations were studied from the longitudinal multicentre Genetic FTD Initiative. Assessments in GENFI included resting-state functional MRI and neuropsychological and clinical assessments. These were repeated annually or biannually, with longitudinal data up to 7 years. We compared functional network dynamics between groups, with clinical severity and with longitudinal clinical progression. We quantified network dynamics by hidden Markov models.

Results

One network state distinguished patients from controls, corresponding spatially to the salience network. There was an increase in salience network occupancy in both cohorts of symptomatic patients, with salience state occupancy associated with clinical and neuropsychological markers of disease severity. We found increased salience state occupancies of presymptomatic mutation carriers who subsequently converted to the symptomatic phase during follow up, and increased rates of cognitive and clinical decline in both symptomatic and older presymptomatic participants with higher salience state occupancies.

Conclusion

Changes in network dynamics in frontotemporal dementia are associated with cognitive decline and conversion to symptomatic disease.

Conflicts of interest

No interests to declare