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Distinct patterns of cerebrovascular reactivity alterations in pre-symptomatic and symptomatic familial frontotemporal dementia

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State of the art: Familial frontotemporal dementia (FTD) can arise from mutations in the C9orf72, GRN or MAPT genes. While brain atrophy and blood perfusion decreases have been identified in symptomatic and pre-symptomatic mutation carriers, the impact of mutations on cerebrovascular reactivity (CVR) is unknown. The CVR indicates the ability of cerebral blood vessels to dynamically regulate blood supply and is indicative of cerebrovascular health. CVR can be measured safely, reliably and at scale from resting-state fluctuation amplitudes (RSFA). Here we use RSFA to quantify CVR in symptomatic and pre-symptomatic FTD.

Methodology: In the Genetic FTD Initiative (GENFI) cohort, cross-sectional RSFA differences between pre-symptomatic (n=287) and symptomatic (n=127) carriers, and non-carriers (n=266), were examined using robust regression on voxel-based and independent component-based maps. We tested the moderating effect of genetic status on the relationship between age and RSFA.

Results: Compared to non-carriers, symptomatic carriers exhibited significant RSFA *reductions* in frontal cortex, including right superior frontal gyrus, left middle frontal gyrus, right insula and left posterior cingulate cortex. In contrast, pre-symptomatic carriers showed RSFA decreases in posterior parietal cortex, compared to non-carriers. There was a stronger age-related decline in RSFA for gene carriers *versus* non-carriers over much of the frontal cortex.

Conclusion: These findings indicate that loss of CVR in pre-symptomatic and symptomatic subjects follows a spatially distinct pattern, suggesting that RSFA may provide additional value in understanding the interaction between cerebrovascular health, latent neuropathology, and its progression in people with FTD-associated mutations.

Conflicts of interest

The author declares no conflicts of interest.