

Functional connectivity from disease epicenters in frontotemporal dementia

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State of the art. In this study, we used a novel graph-theory-based MRI paradigm to explore functional connectivity reorganization at increasing topological distance from disease epicenters and its relationship with atrophy in frontotemporal dementia (FTD) variants.

Methodology. Patients with behavioral variant of FTD (bvFTD, n=64), non-fluent (nfvPPA, n=34) or semantic variant of primary progressive aphasia (svPPA, n=36) and 94 healthy controls underwent 3T MRI. Peaks of atrophy of each variant (i.e., disease epicenters) were identified in an independent cohort of 42 cases with high confidence of FTLD pathology and used as seed regions for stepwise functional connectivity (SFC) analyses.

Results. The identified disease epicenters were the left anterior insula for bvFTD, left supplementary motor area for nfvPPA, and left inferior temporal gyrus (ITG) for svPPA. Compared with controls, bvFTD and nfvPPA patients showed widespread decreased SFC in bilateral cortical regions with direct/indirect connections with the epicenters, and increased SFC either in circumscribed regions close to the respective seed region or in more distant cortical and cerebellar areas. Across all link-steps, svPPA showed SFC decrease localized in the temporal lobes. Topological distance from the left ITG in controls correlated with regional grey matter volume in svPPA patients.

Conclusions. Our findings demonstrate that each FTD syndrome is associated with a characteristic interplay of decreased and increased functional connectivity with the disease epicenter, affecting both direct and indirect connections.

Funding. Italian Ministry of Health (GR-2011-02351217); European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease; US National Institutes of Health (R01-DC010367, R01-DC12519, R01-DC14942, R01-NS89757, R21-NS94684).

Conflicts of interest

No conflicts of interest