Altered functional brain connectome in the behavioral variant of frontotemporal dementia

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Background. Topology-based analysis of the human brain networks offers a novel avenue for assessing the patterns of functional disconnection in neurodegenerative diseases.

Objective. To examine whether, how and to what extent the functional organization of the human brain connectome is disrupted in patients with the behavioral variant of frontotemporal dementia (bvFTD). The correlations between network property changes and cognitive variables were also tested.

Methods. Graph theoretical analysis was applied to resting state functional MRI (RS fMRI) data from 18 bvFTD patients and 50 healthy matched elderly individuals. Functional connectivity between 90 cortical and subcortical brain regions was estimated using bivariate correlation analysis and thresholded to construct a set of undirected graphs.

Results. The global topological organization of the functional brain network in bvFTD patients was significantly disrupted as indicated by reduced small-world properties, reduced global efficiency and increased assortativity relative to normal elderly subjects. Compared with controls, bvFTD retained their major "hub" regions in the medial parietal, temporal and occipital lobes, but cortical hubs were not indicated in the frontal lobes (Figure). A decreased nodal centrality was also found in the left caudate nucleus, left insular cortices and some parts of the temporal lobes bilaterally. BvFTD patients showed the greatest decrease in inter-regional connectivity between the insular cortices and subcortical, temporal and frontal regions. Furthermore, in bvFTD patients, the alterations of various global network properties significantly correlated with executive function deficits.

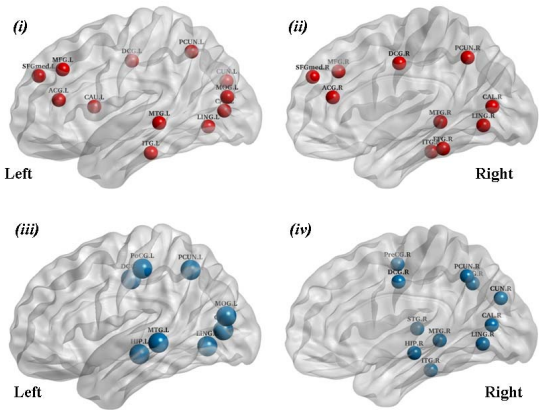

Figure. Brain cortical hubs of the functional networks of healthy controls (*i*, *ii*) and patients with bvFTD (*iii, iv*). Hubs were identified as brain regions having either integrated nodal degree or betweenness centrality one standard deviation greater than the network average.

Conclusions. Our findings show that the global and local functional network is altered in bvFTD patients, suggesting a loss of efficiency in information exchange between both distant and close brain areas. The altered brain regions are mainly located in those structures that are closely associated with the neuropathological changes in bvFTD. It would appear that aberrant topology of the functional brain networks in bvFTD underlies cognitive deficits in these patients.