Network disruption in Alzheimer's disease and behavioural variant frontotemporal dementia

Philipp Loske[1], Alison Murray[1], Claude Wischik[2,3], Vesna Vuksanović[1]
1 Aberdeen Biomedical Imaging Centre, University of Aberdeen, Aberdeen, UK
2 TauRx, Therapeutics, Aberdeen, UK
3 School of Medicine and Dentistry, University of Aberdeen, Aberdeen, UK

Introduction

Aim: (i) To investigate differences in the *default mode network* (DMN) and *salience network* (SLN) in Alzheimer's disease (AD) and behavioural variant frontotemporal dementia (bvFTD) using structural MRI (ii) To test involvement of two other networks, *central executive network* (CEN) and *semantic appraisal network* (SAN), in these connectivity changes.

Motivation: AD and bvFTD are neurodegenerative syndromes, characterized by involvement of brain networks. Previous studies have demonstrated divergent network connectivity changes in DMN and SLN. CEN and SAN are known to support different cognitive functions impaired in AD and bvFTD.

Participants and Methods

Participants: 200 randomly selected subjects from a large sample of patients with AD (N=1614) and bvFTD (N=213) as part of a clinical trial. 200 healthy older adults selected as control group.

Imaging data: three-dimensional, T1-weighted magnetic resonance imaging (MRI)

Image preprocessing and analysis: FreeSurfer 5.3.0 (`https://surfer.nmr.mgh.harvard.edu/`)

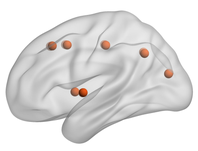
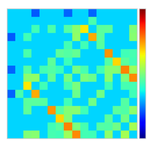
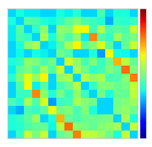
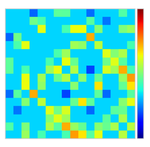
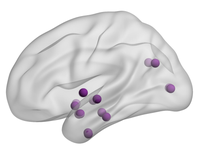
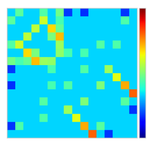
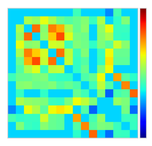
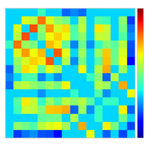
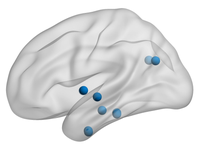
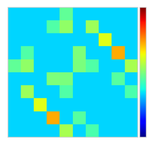
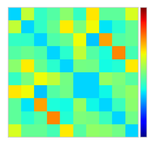
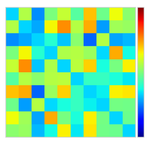
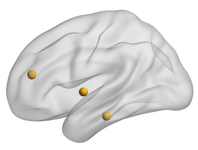
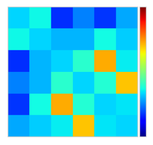
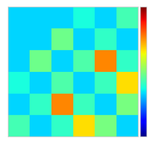
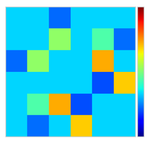
Network construction: group-level **cortical networks** estimated from regional volumes:

- Nodes: brain parcellation into 68 cortical and 20 subcortical regions (Desikan-Kiliany atlas)
- Edges: partial cross-correlation values between *cortical volumes* (averaged over each region) across all subjects within one group, controlling for *age*, *gender* and *total brain volume*

Network properties: **node strength** of network correlations (i.e., average weight of positive correlations), **clustering coefficient** (i.e., measures how well groups of neighbouring nodes are connected)

Statistics: Significance tested with non-parametric *Kruskal-Wallis test* and post-hoc correction with Bonferroni test

Network Construction

	Function and involvement	Spatial visualisation (lateral view (L))	correlation networks: controls	AD	bvFTD
DMN	- Involved in non-focused activity, thinking about others, imagining the future - Known to be disrupted in AD [3]				
SLN	- responsive to emotional stimuli - known to be inversely correlated with DMN - Affected in bvFTD [2]				
CEN	- involed in problem solving, reasoning, decision-making, working memory - Affected in AD [4]				
SAN	- active during tasks involving semantically driven personal evaluation - Associated with bvFTD [2]				

Regions

Region	DMN	SLN	CEN	SAN
corpus callosum (cc) central		×		×
cc mid posterior	×			
lh and rh accumbens		×		
lh and rh amygdala		×		
lh hippocampus		×		×
rh hippocampus		×	×	
lh putamen	×			
lh and rh caudalmiddlefrontal	×			
lh and rh cuneus	×			
lh and rh entorhinal		×	×	
lh and rh inferiorparietal		×	×	
lh and rh insula	×	×	×	×
lh and rh parahippocampal			×	
lh and rh parsopercularis	×			
lh pericalcarine		×		
lh and rh postcentral	×			
lh and rh precuneus	×			
lh and rh rostralmiddlefrontal				×
lh and rh superiorfrontal	×			
lh superiortemporal		×	×	

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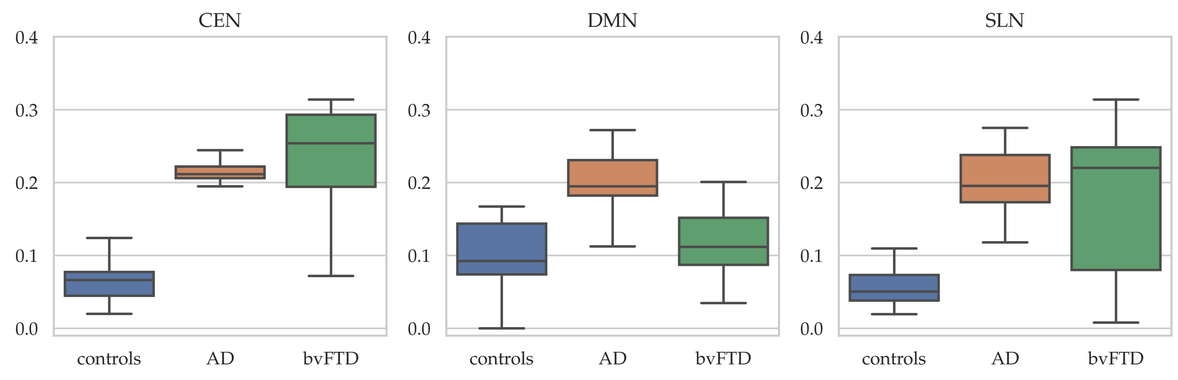
Regions of corpus calossum are not displayed in spatial visualisation

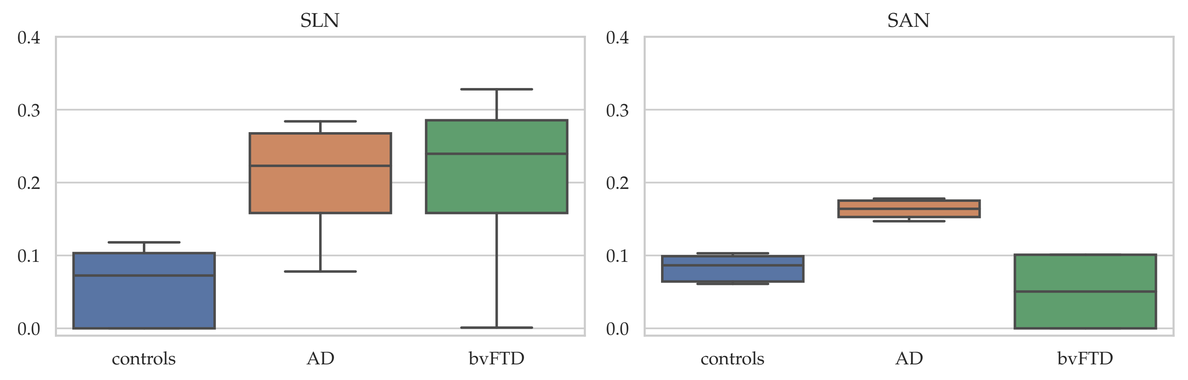
Results - Node Strength



- node strength higher in AD and bvFTD compared to controls ($p < 0.01$)
- DMN: node strength higher in AD compared to bvFTD and controls ($p < 0.01$)
- SLN: node strength higher in AD and bvFTD compared to controls ($p < 0.01$)

No significant differences in SAN.

Results - Clustering Coefficient



- SLN: clustering higher in AD and bvFTD compared to controls ($p < 0.01$)
- SAN: clustering higher in AD compared to bvFTD ($p = 0.017$) and controls ($p < 0.01$)

No significant differences in CEN and DMN.

Conclusion

We found significant differences in node strength and clustering coefficient in all four functional networks between the two patient groups and healthy controls, showing that the network integrity of different functional networks in the brain are affected differently depending on the type of dementia. These results may provide complementary neuroimaging marker for differentiating diagnosis between bvFTD and AD.

Acknowledgement

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2020 SINAPSE ASM, June 19; email: p.loske.18@abdn.ac.uk