

Salience and Default Mode Network Connectivity Changes in Frontotemporal Dementia

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INTRODUCTION

FTD is a clinically heterogeneous disorder with behavioural and language variant subtypes. Progressive breakdown of neural networks measurable through connectivity analyses is a key pathophysiological feature of FTD¹. We focused on identifying alterations in Salience (SN) and Default Mode (DMN) networks, as these have not before been studied in detail across the different FTD clinical phenotypes and genetic mutations.

METHODS

We performed task-free functional MRI (fMRI), using either a Siemens Trio or Prisma 3T scanner, on 81 patients with FTD and 24 age- and gender-matched controls, using the precuneus (DMN), and left anterior insula cortex (SN) as regions-of-interest for seed-based connectivity analysis. Cross-sectional analyses stratified patients by disease (30 behavioural variant FTD, bvFTD; 13 logopenic variant, lvPPA; 22 nonfluent variant, nfvPPA; and 16 semantic variant, svPPA) or genetic diagnosis (sporadic, *C9orf72*, *GRN* or *MAPT*). Registration to anatomical T1 MPRAGE scans, functional preprocessing, motion and non-neuronal physiological denoising, and analysis was conducted using SPM12 and the CONN toolbox. Connectivity in the DMN and SN were explored by incorporating the BOLD time series into a general linear model, correcting for age, gender and scanner type. Healthy controls were compared with each diagnostic subgroup to determine significant between-group resting-state network alterations. T maps from GLM group comparisons are displayed with an uncorrected peak height ($p < 0.005$) and FWE-corrected cluster height ($p < 0.05$) threshold.

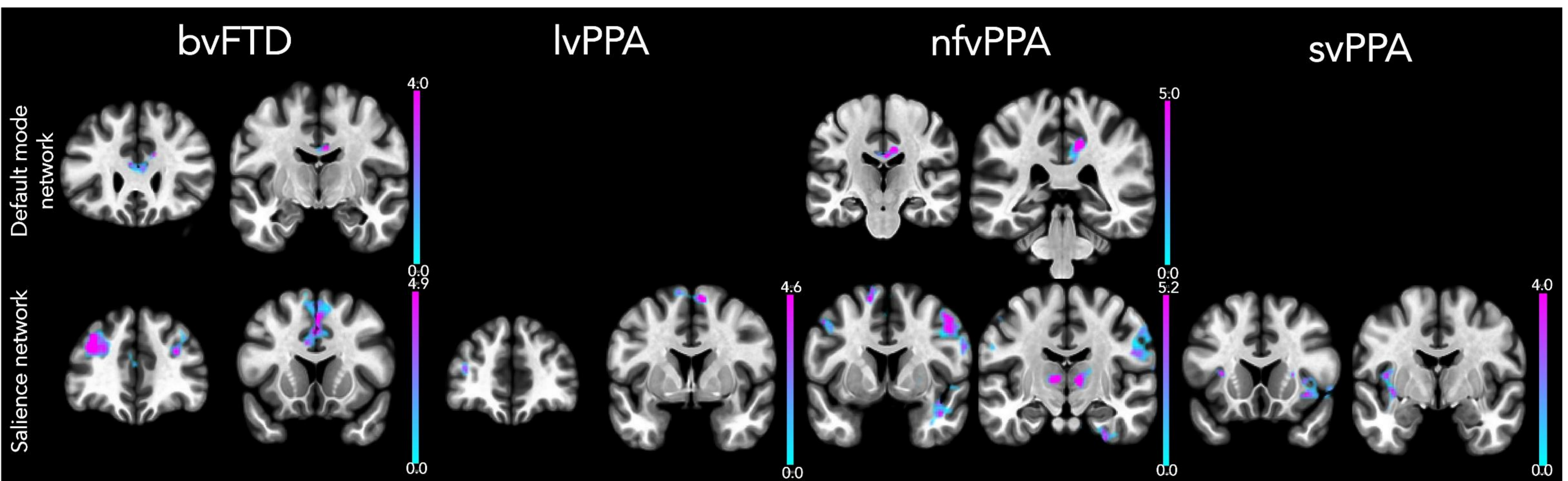


Figure 1. The four clinical syndromes demonstrated divergent patterns of reduced functional connectivity compared to controls.

RESULTS

Clinical phenotypes. Decreased connectivity was seen in parts of the DMN, surviving FWE-correction for multiple comparisons, in both bvFTD and nfvPPA in the cingulate and right ventromedial prefrontal cortex. All subgroups had decreased connectivity in the SN, predominantly in the prefrontal and insula cortices (fig. 1). In bvFTD these reductions were predominantly located in the bilateral superior frontal gyrus and right paracingulate gyrus. Connectivity reductions were seen in each of the PPA subgroups: in the superior frontal gyrus (lvPPA), superior, inferior and middle frontal gyri, thalamus, and insula (nfvPPA) and bilateral insula cortices (svPPA) (fig. 1).

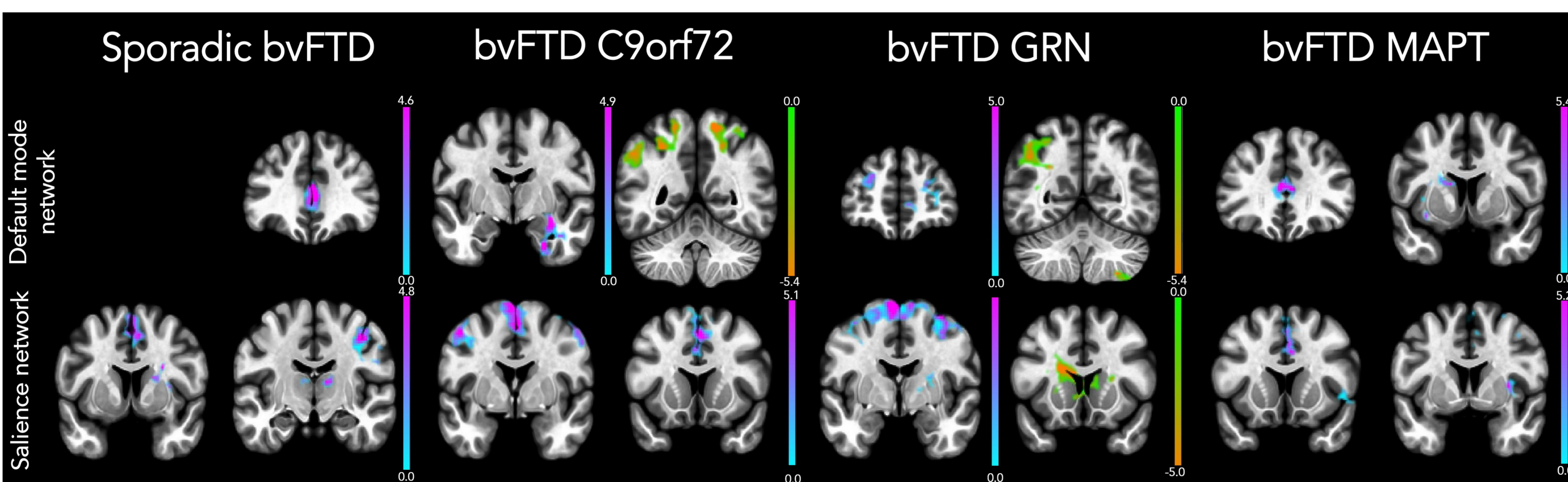


Figure 2. Altered functional connectivity in three bvFTD mutation groups compared to controls.

Genetic mutations. *C9orf72* and *GRN* mutation carriers showed enhanced DMN connectivity, mainly posteriorly. Salience network connectivity was reduced significantly in prefrontal regions in both groups. Reduced connectivity in the DMN and SN of *MAPT* mutation carriers primarily occurred in the anterior cingulate and insula (fig. 2).

CONCLUSION

Bilateral prefrontal reductions in connectivity in the SN and DMN are common to all FTD phenotypes¹. However, different patterns of connectivity alterations can be seen during subanalysis of diagnostic groups, including PPA and mutation subtypes².

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