# Exploring early changes in brain morphology in frontotemporal dementia

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## Research

Frontotemporal dementia (FTD) refers to a collection of younger-onset dementia syndromes which strike individuals in their 50-60's, producing stark changes in behaviour and personality, language and/or motor skills. These changes reflect the progressive degeneration of frontal and/or temporal regions in the brain that support complex functions such as decision-making, personality, social cognition, and language. With no treatments to halt or slow the progression of FTD, individuals become severely impaired in everyday functioning and increasingly dependent on family members.

A major barrier to the accurate diagnosis and management of FTD is its misdiagnosis as a psychiatric problem or as an atypical variant of Alzheimer's disease (AD). In this light, neuroimaging techniques are becoming increasingly important for the early diagnosis of FTD. Current imaging metrics, however, only partially capture the structural complexity of the cerebral cortex and show poor sensitivity to detect subtle brain changes in early stages of the disease course.

With the support of the Brain Foundation, we sought to use new developments in neuroimaging to improve the diagnosis of FTD. We proposed that the natural folding of the cerebral cortex represents a clinically useful biomarker for the early detection of FTD. Specifically, we sought to establish whether a measure of cortical folding complexity (fractal dimensionality) could serve as a new biomarker for structural brain changes in FTD. We predicted that overall fractal dimensionality would be significantly lower in FTD and Alzheimer's disease versus Controls, but that disease-specific differences would be evident in distinct regions of interest. Specifically, we predicted that alterations in cortical folding would be most pronounced in frontal and insular cortices in the FTD group.

## Outcome

We recruited 30 behavioural variant FTD (bvFTD), 30 Alzheimer's disease (AD) and 30 healthy older Control participants for this study. Participants were matched for age, sex, and years in formal education. Patient groups were matched for level of cognitive and functional impairment. Using Madan's fractal dimensionality analysis methods, we found significant differences in the surface topology of the two types of dementia. A predominantly right-sided frontoinsular profile was found in bvFTD relative to AD, while the reverse contrast implicated a largely posterior parietal and temporo-occipital network. Importantly, we found a robust association between fractal dimensionality of the insula and emotion processing disturbances in bvFTD. This finding converges with a large body of evidence to implicate the insula as one of the key early drivers in the social and emotional symptoms that typify the bvFTD syndrome.

This work is ongoing, and we are currently exploring new exciting applications of this technique. One such avenue is to determine how changes in cortical complexity differ across FTD patients with different underlying genetic mutations (e.g., *C9orf72*, MAPT, GRN). Given the intense global effort to discover clinically sensitive imaging biomarkers, our findings represent an important step forward in improving the early and accurate diagnosis of FTD.