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Longitudinal patterns of cortical thinning in behavioural variant frontotemporal dementia

Elizabeth Gordon[1], Jason D. Warren[1], Sebastien Ourselin[2], Nick C. Fox[1], Jonathan D. Rohrer[1]

1. Dementia Research Centre, Institute of Neurology, University College London, UK. 2. Centre for Medical Image Computing, University College London, UK.

Introduction

Characteristic magnetic resonance imaging (MRI) abnormalities have been shown in cross-sectional studies of behavioural variant frontotemporal dementia (bvFTD) but little is known about patterns of change over time in this highly heterogeneous patient population. Advancing our understanding of longitudinal patterns of disease progression will be important for improved diagnosis, prognosis and clinical trial stratification.

Methods

Subjects: The patient cohort consisted of 30 bvFTD subjects who had undergone three serial volumetric T1-weighted MRI scans. Mean (standard deviation (SD)) disease duration at baseline was 4.6 (3.2) years. Mean (SD) interval from Scan 1–2 was 1.64 (1.8) years and 1.17 (0.8) years for Scan 2–3. 76 healthy age-matched individual were included in the control cohort.

Image Analysis: All volumetric MRI underwent an automated technique for cortical thickness measurement using Freesurfer (http://freesurfer.net/). This set of tools allows for the demarcation of white and grey matter surfaces and subsequent calculation of the cortical thickness between[1]. All segmentations were visually inspected by an experienced image analyst and edited where required. Maps demonstrating statistically significant differences between bvFTD and control cohorts were produced, controlling for age, gender, scanner strength and FDR corrected for multiple comparisons (Figure 1.).

Results

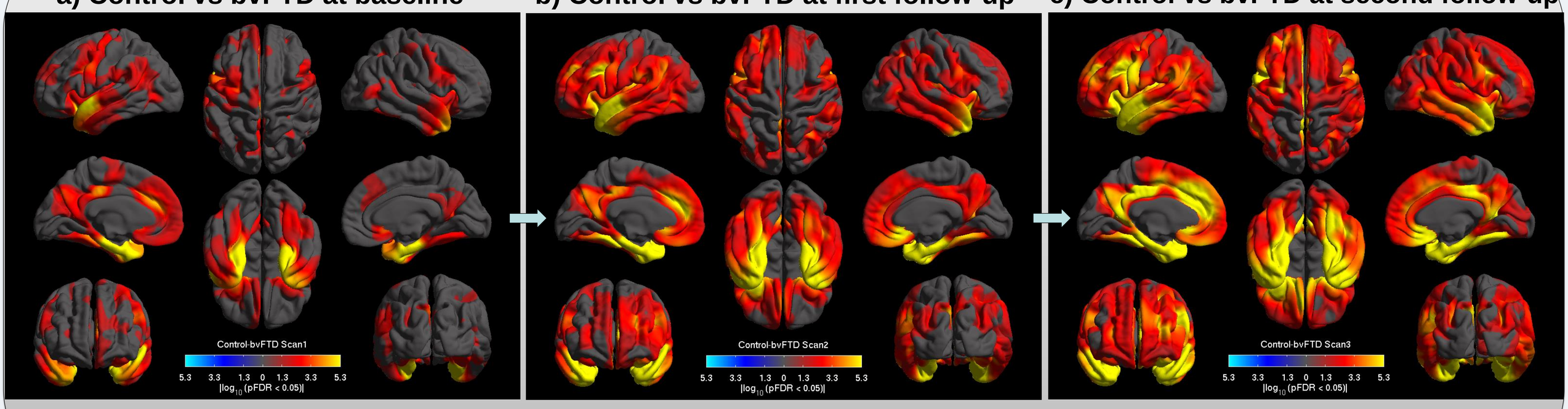


Figure 1: Progression of regional cortical thinning in bvFTD subjects compared with healthy controls at a) baseline (scan1) b) first follow-up visit (scan 2) and c) second follow-up visit (scan 3). The colour coding for P-values is on a logarithmic scale and FDR corrected at p<0.05. Warmer colours (positive values) represent regions of significant cortical thinning while cooler colours (negative values) represent cortical thickening.

Baseline (scan 1):

At baseline, peak areas of cortical thinning included the entorhinal cortices (23% thinner than controls bilaterally), temporal poles (17% right, 19% left) and parahippocampal cortices (12% right, 15% left). Significant cortical thinning was also detected in the precentral gyrus (8% right, 10% left), anterior cingulate (4% right, 9% left), orbitofrontal lobe (6% bilaterally) and insula (6% right, 8% left).

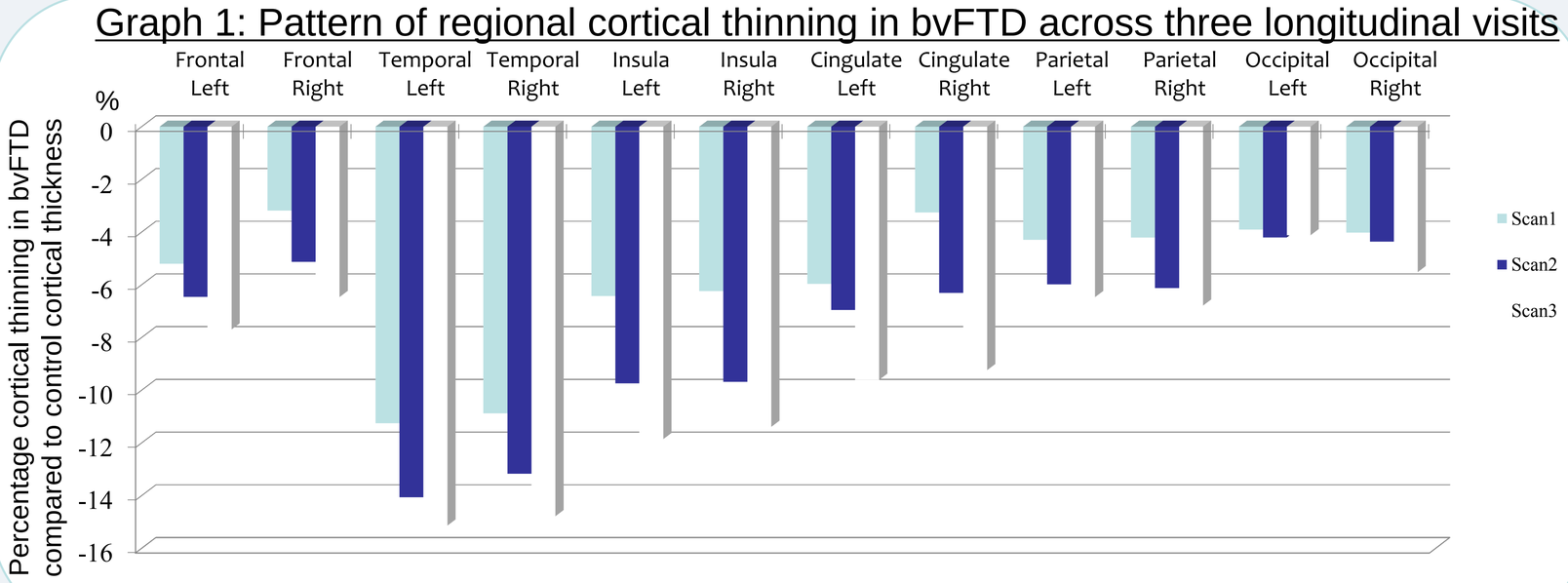
First follow-up Session (scan 2)

At follow-up, these areas showed further reduction, with thinning spreading more posteriorly in the cingulate and temporal lobes and through prefrontal areas (pars triangularis (4% right, 7% left) and pars opercularis (7% right, 6% left)), inferior parietal lobe (6% bilaterally) and precuneus (7% right, 6% left).

Second follow-up Session (scan 3)

By the third visit (2.8 (2.1) years following the baseline examination), thinning was evident in all cortical areas with the occipital and superior parietal lobes remained relatively spared even at this late stage of the disease process. The pattern of progression was relatively symmetrical across all three visit comparisons.

Graph 1: Pattern of regional cortical thinning in bvFTD across three longitudinal visits



Conclusions

The pattern of disease progression in bvFTD is associated with bilateral spreading of cortical thinning from initial anterior areas in the insula, cingulate, frontal and temporal lobes to more posterior areas but with relative sparing of superior parietal and occipital lobes even late in the disease course. This work confirms and extends previous cross-sectional investigations of disease progression in bvFTD.

References: **1.** Fischl B, Sereno MI, Dale AM. Cortical surface-based analysis. II: inflation, flattening, and a surface-based coordinate system. *Neuroimage* 1999; 9: 195–207

Acknowledgements: The Dementia Research Centre is supported by Alzheimer's Research UK, Brain Research Trust, and The Wolfson Foundation. This work was also supported by funding from the UK Medical Research Council, Wellcome Trust and NIHR Queen Square Biomedical Research Unit. JDR is supported by an NIHR Rare Disease TRC Fellowship. EG is supported by an Alzheimer's Society PhD Studentship.