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Hypothalamic atrophy in behavioural variant frontotemporal dementia and its relationship to eating behaviour

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Background

Abnormal eating behaviours such as hyperphagia and craving for sweet foods are frequently reported in behavioural variant frontotemporal dementia (bvFTD). The hypothalamus is the regulatory centre for feeding and satiety but its role in bvFTD has not been fully clarified, partly due to its difficult identification on magnetic resonance images (MRIs).

Methods

We aimed to investigate the hypothalamic volumetry and its shape in a sample of 18 bvFTD patients with abnormal eating behaviour (assessed with the revised version of the Cambridge Behavioural Inventory, CBI-R) compared to 19 cognitively-normal controls. Three different techniques were used: i) voxel-based morphometry (VBM); ii) global volumetry with a novel optimized multimodal manual segmentation protocol, developed using 3D T1 and T2-weighted MRIs at 3T (intrarater intraclass correlation coefficients ≥0.93); iii) shape analysis using spherical harmonic-point distribution model (SPHARM-PDM).

Results

No significant differences were found in age (mean 60, standard deviation 12) and education between groups, while controls and patients differed in gender (p=0.038, Chisquare test), MMSE and CBI-R (p=0.009 and p<.0005, Mann-Whitney U test). The bvFTD group showed a 17% reduction in hypothalamic volume compared with controls. MAPT mutation carriers showed a trend for lower volumes on both sides compared with C9orf72 (12% difference). **Table.**

	bvFTD (n=18)	Controls (n=19)	% difference	*p-value*
Hypothalamus R, mm^3	398 (62)	476 (38)	-16%	**<0.0005**
Hypothalamus L, mm^3	385 (53)	465 (39)	-17%	**<0.0005**

	bvFTD-MAPT (n=9)	bvFTD-C9orf72 (n=6)	% difference	*p-value*	*p-value vs Controls*
Hypothalamus R, mm^3	380 (73)	436 (41)	-13%	0.088	**MAPT: 0.001** **C9orf72: 0.050**
Hypothalamus L, mm^3	375 (63)	418 (31)	-10%	0.224	**MAPT: 0.001** **C9orf72: 0.025**

Table. Hypothalamic volumetry corrected for total intracranial volume (TIV). *Values denote mean (Standard Deviation). P-values denote significance on Mann-Whitney U test.*

VBM revealed the typical pattern of grey matter atrophy in bvFTD in the frontal, orbitofrontal, temporal, insular and (posterior and anterior) cingulate cortices, together with thalamic area (p<0.001 FDR corrected). As visible from the **Figure 1**, the hypothalamic area was affected.

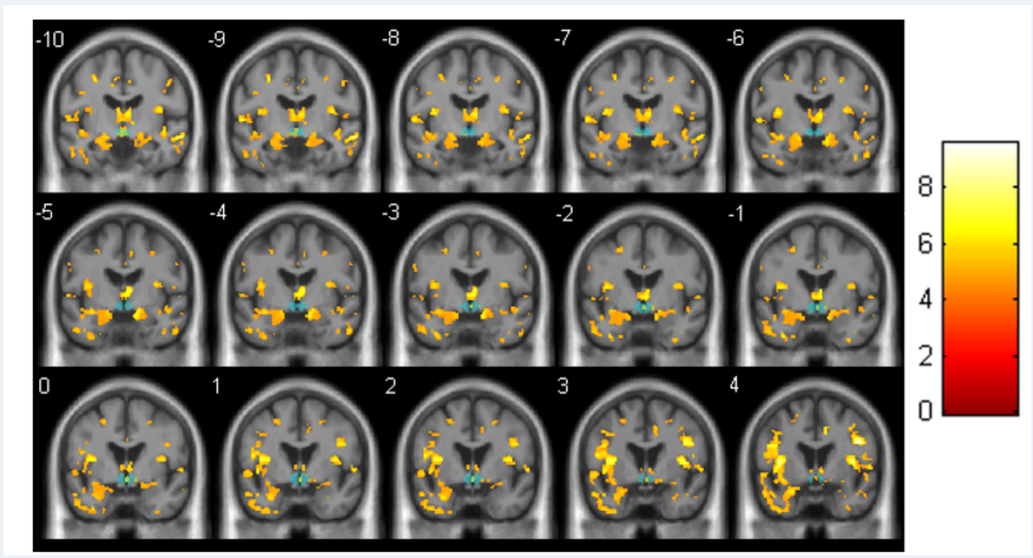

Figure 1. Voxel-based morphometry analysis in 18 bvFTD patients compared to 19 controls. *The selection of coronal slices shows the hypothalamic area in light blue. Analyses were adjusted for age, sex and TIV. The colour bar indicates the t-values.*

We found a significant shape deflation in bvFTD patients, compared to controls, which was mainly localized on the medial hypothalamus. **Figure 2**.

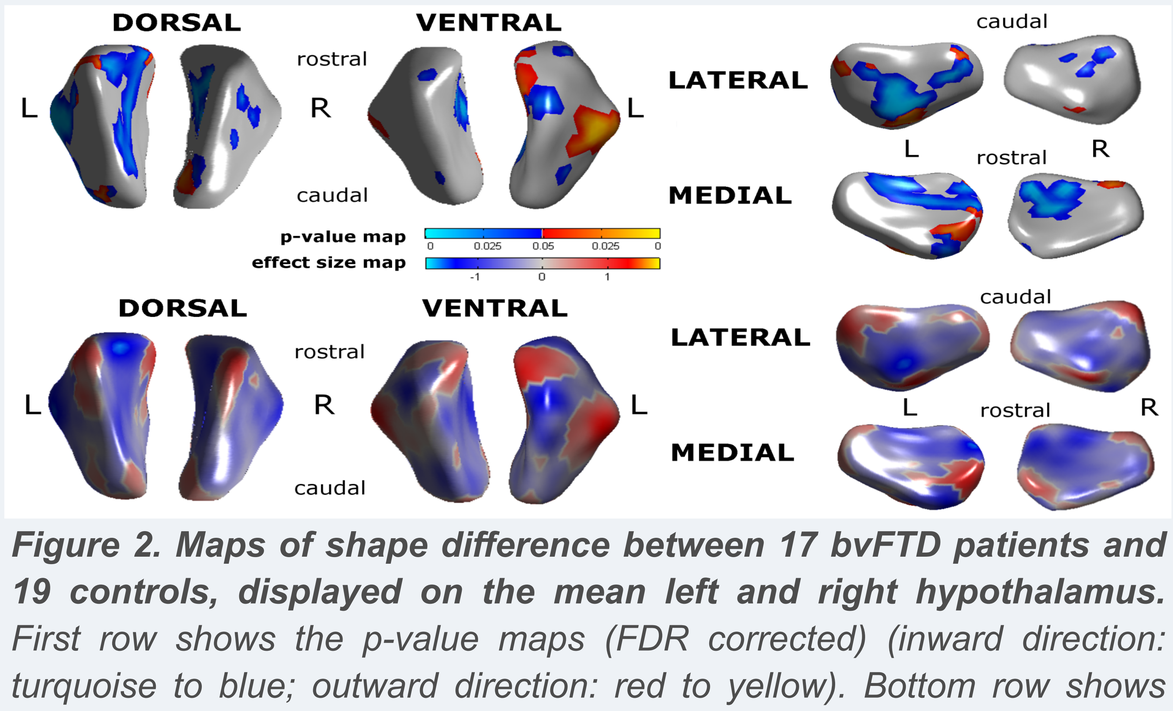

Figure 2. Maps of shape difference between 17 bvFTD patients and 19 controls, displayed on the mean left and right hypothalamus. *First row shows the p-value maps (FDR corrected) (inward direction: turquoise to blue; outward direction: red to yellow). Bottom row shows effect size maps. Analyses were adjusted for age, sex and TIV.*

The CBI-R "Eating habits" sum of scores had a significant effect on the hypothalamic volumes in the bvFTD group (p≤0.028, ANOVA), No significant correlations were found between the CBI-R subscores or single items and hypothalamic volume, shape and VBM data.

Conclusions

In summary, bvFTD patients showed lower hypothalamic volumes compared with controls, localized in the subnuclei which regulate food intake, reward and perception of satiety. Moreover, different genetic mutations seem to have a differential impact on the hypothalamus.

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. MB is supported by Guarantors of Brain for the attendance at the Conference.