**Detailed structural analysis of the hypothalamus in behavioural variant frontotemporal dementia**

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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 investigated hypothalamic volume and shape in a sample of 18 bvFTD patients (including 9 MAPT mutation carriers and 6 C9orf72 expansion carriers) with abnormal eating behaviour compared with 18 cognitively-normal controls. All participants were scanned on a 3T Siemens Trio, and the presence of abnormal eating behaviour was assessed with the revised version of the Cambridge Behavioural Inventory (CBI-R). A novel optimized multimodal manual segmentation protocol of the whole hypothalamus was developed using 3D T1 and T2-weighted MRIs (intrarater intraclass correlation coefficients ≥0.93). The whole hypothalamus was subsequently segmented manually into five different subunits (Figure 1). Shape differences were investigated using the SPHARM-PDM toolbox.

**Results**

The bvFTD group showed a 17% reduction in hypothalamic volume compared with controls ($p<0.005$, Mann-Whitney U test): right, mean 398 (standard deviation 62) versus 477 (38) $mm^3$ and left, 385 (53) versus 467 (39) $mm^3$, corrected for total intracranial volume. MAPT mutation carriers showed a trend for lower volumes on both sides compared with C9orf72 (12% difference). Specifically, in both shape and volumetric analyses, we found a strong evidence for the involvement of the dorsal tuberal hypothalamus in bvFTD patients, compared with controls (Figure 2). No significant correlations were found with the clinical scores.

**Conclusions**

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