Phenomenology and anatomy of abnormal behaviours in frontotemporal dementia as measured by the Cambridge Behavioural Inventory

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BACKGROUND

The Cambridge Behavioural Inventory (CBI) is an informant-based questionnaire, which allows profiling of behavioural and neuropsychiatric deficits in patients with dementia. These changes are defining features of behavioural variant frontotemporal dementia (bvFTD), however, studies of the neural correlates and differential profiles of these changes across the full FTD spectrum are currently lacking.

METHODS

Eighty-three FTD patients were recruited to the study (Table 1), including 37 with bvFTD, 21 with semantic variant primary progressive aphasia (svPPA) and 25 with nonfluent variant PPA (nfvPPA). Primary caregivers completed the revised version of the CBI (CBI-R) and scores for the 10 domains were converted to percentage of maximum score (Figure 1). Domain scores were compared between FTD groups using linear regression models, correcting for age, gender and disease duration. All 83 patients also underwent T1-weighted 3D volumetric imaging on a 3T Siemens Trio scanner. Neural correlates associated with each CBI-R domain were investigated using a voxel-based morphometry (VBM) analysis in SPM12. Analyses included age, gender and total intracranial volume (TIV) as covariates and corrected for multiple comparisons using adjustment for false discovery rate (FDR).

RESULTS – VBM

Neural correlates of behavioural deficits differed across the CBI-R domains. *Memory and Orientation* score correlated with bilateral orbitofrontal and medial temporal lobe atrophy (right > left), whilst *Self Care* correlated predominantly with atrophy in the orbitofrontal lobe, insula, thalamus and cingulate cortex bilaterally. Scores for *Stereotypic and Motor Behaviours* correlated with atrophy throughout the temporal lobe with cingulate cortex involvement (right > left) as well, whilst *Motivation* scores were associated with reduced volume in the orbitofrontal and medial temporal lobes, thalamus and posterior cingulate cortex bilaterally (Figure 2). No significant correlations were seen in the other CBI-R domains after FDR correction for multiple comparisons.

	bvFTD (*n* = 37)	svPPA (*n* = 21)	nfvPPA (*n* = 25)
Gender (M / F)	31 / 6	9 / 11	10 / 15
Age at assessment (yrs)	63 6 (7.4)	65.6 (6.8)	69.9 (6.5)
Age at onset (yrs)	57.2 (7.6)	59.1 (6.7)	65.4 (6.2)
Disease duration (yrs)	6.4 (4.3)	6.4 (2.5)	4.6 (2.5)

Table 1. Patient demographics of the cohort by clinical diagnosis. *Mean (standard deviation) unless stated.*

RESULTS – LINEAR REGRESSION

The bvFTD group showed the greatest deficits across domains, followed by svPPA and then nfvPPA. Comparing bvFTD and nfvPPA, deficits were significantly more severe in bvFTD group for the *Memory and Orientation*, *Abnormal Behaviour*, *Eating habits*, *Stereotypic and Motor behaviours* and *Motivation* domains. These five domains were also significantly more affected in svPPA compared with nfvPPA with the addition of the *Beliefs* domain. The only significant difference between the bvFTD and svPPA groups was in the *Eating habits* domain with bvFTD patients having a greater deficit.

	Memory and Orientation	Everyday Skills	Self Care	Abnormal Behaviour	Mood	Beliefs	Eating Habits	Sleep	Stereotypic and Motor Behaviours	Motivation
bvFTD vs svPPA	NS -0.4 [-15.0, 14.2]	NS -6.8, -23.6, 9.9]	NS 0.8 [-14.5, 16.1]	NS -11.4 [-28.3, 5.4]	NS -11.6 [-26.0, 2.9]	NS 4.0 [-11.0, 3.0]	**p = 0.034 -16.2 [-31.2, -1.3]**	NS -7.8 [-26.1, 10.6]	NS 3.8 [-14.5, 22.2]	NS -3.5 [-20.8, 13.7]
bvFTD vs nfPPA	**p < 0.001 -32.2 [-47.8, -16.7]**	NS -5.6, [-25.1, 14.0]	NS -4.5 [-16.9, 7.9]	**p < 0.001 - 30.4 [-44.8, -16.1]**	NS -6.0 [-22.2, 10.3]	NS -9.7 [-19.5, 0.1]	**p = 0.040 - 21.0 [-40.8, -1.1]**	NS -15.7 [-39.0, 7.6]	**p < 0.001 - 35.2 [-52.7, -17.7]**	**p < 0.001 - 33.6 [-55.4, -11.7]**
nfvPPA vs svPPA	**p < 0.001 33.1 [14.5, 51.6]**	NS -8.9 [-26.6, 8.7]	NS 5.1 [-8.3, 18.5]	**p = 0.010 13.1 [3.3, 22.9]**	NS -5.2 [-17.1, 7.3]	**p = 0.023 7.8 [1.1, 14.5]**	**p = 0.015 19.0 [3.9, 34.2]**	NS 9.4 [-7.8, 26.5]	**p < 0.001 37.2 [21.5, 52.9]**	**p = 0.020 21.8 [3.6, 39.9]**

Table 2. Linear regression comparing subgroups across CBI-R domains. Analyses were corrected for age, gender and disease duration. Differences between groups with 95% confidence intervals are shown. NS = not significant

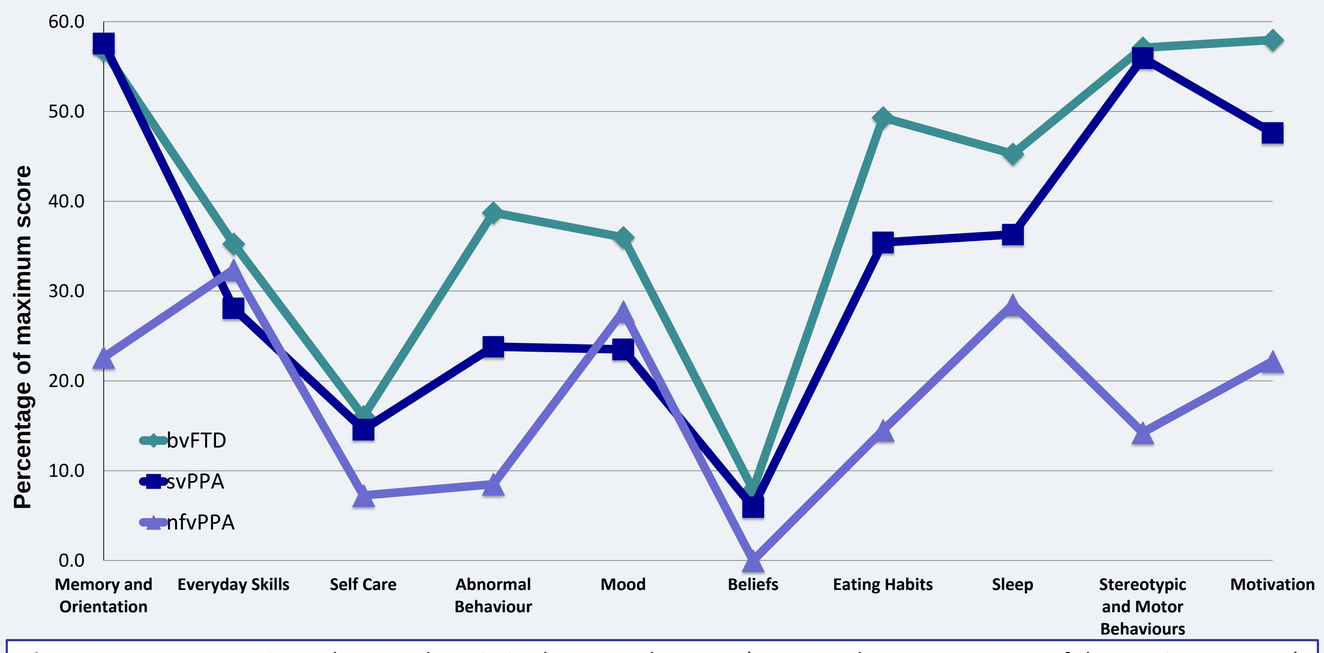

Figure 1. Mean scores in each CBI-R domain in the FTD subgroups (presented as a percentage of the maximum score)

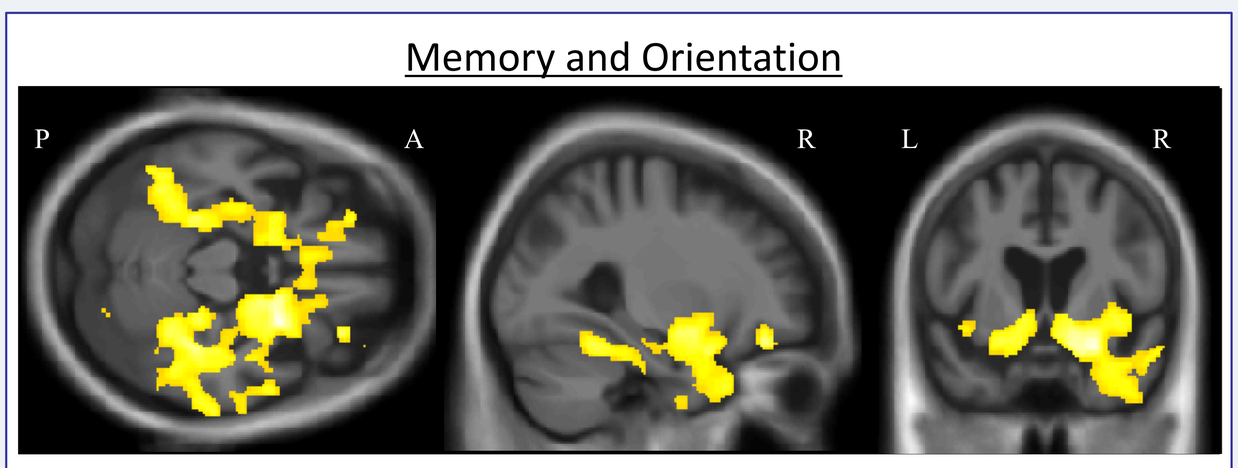

Figure 2. Voxel-based morphometry analyses showing regions of reduced volume associated with increased deficits captured by CBI-R domain scores. Clusters are overlaid on a template produced from averaging all patients included in the analysis. Results are shown with FDR correction for multiple comparisons.
R = Right, L = Left, A = Anterior, P= Posterior, M = Midline.

CONCLUSIONS

The CBI-R captures differences in behavioural deficits between the FTD syndromes, with the different domains demonstrating distinct neural correlates.

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