

Investigating the role of brief cognitive assessments in the diagnosis of frontotemporal dementia

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Background

The effectiveness of current brief cognitive tests to diagnose individuals with frontotemporal dementia (FTD) is limited as the cognitive phenotype differs from those with other forms of dementia, such as Alzheimer's disease, for whom these tests were originally designed. The Edinburgh Cognitive and Behavioural ALS Screen (ECAS) has been recently designed to be more sensitive to disorders with impaired social cognition and executive dysfunction such as FTD. This study aimed to investigate the ability of the ECAS to detect cognitive changes in FTD, and compare it with three commonly used brief cognitive assessments.

Methods

56 individuals were recruited to the study: 24 with behavioural variant FTD, 22 with the language variant primary progressive aphasia (PPA) and 10 individuals were included who are currently healthy but have a 50% genetic risk of developing FTD (see Table 1). All participants were recruited through the FTD research programme at the Dementia Research Centre, UCL Institute of Neurology. All patients had been diagnosed following standardized clinical assessments according to current diagnostic criteria.

	At-risk		bvFTD		PPA	
	Mean years (SD)	Range	Mean years (SD)	Range	Mean years (SD)	Range
Age:	54.0 (13.8)	29-70	64.9 (6.7)	52-77	69.2 (6.9)	57-86
Education:	15.6 (2.4)	11-18	15.2 (2.8)	11-20	15.4 (2.8)	11-18
Disease duration:	N/A	N/A	7.7 (5.5)	2-23	5.5 (2.2)	3-10
Gender: female: male	7:3		4:20		8:14	

Table 1. Participant Demographics (N/A = not applicable)

Participants were tested using the ECAS and the Mini-Mental State Examination (MMSE), and in a subset of 44 patients, also the Montreal Cognitive Assessment (MoCA) and the Addenbrooke's Cognitive Examination (ACE-III). We used standard cut-off scores for each test to determine abnormal performance, and compare across the four tests.

The ECAS has five subscores assessing specific cognitive domains: language, verbal fluency, executive function, memory and visuospatial skills. We performed two further experiments:

- We compared performance in each of these cognitive domains with performance on a formal neuropsychometric battery including tests of language (the British Picture Vocabulary Scale (BPVS) and the Graded Naming Test (GNT)), executive function (D-KEFS Color-Word Interference Test and the Trail-Making Test (TMT)), memory (Recognition Memory Tests for Faces and Words (RMT) and the Camden Paired Associates Learning test (CPAL)) and visuospatial skills (the Block Design task from the Wechsler Abbreviated Scale of Intelligence (WASI) and the Object Decision subtest of the Visual Object and Space Perception battery (VOSP)).
- We determined the neural correlates of these subscores by performing a voxel-based morphometry (VBM) analysis using all participants' T1-weighted volumetric MRI scans performed on a 3T Siemens Trio Scanner.

Results

Comparison of ECAS with other brief cognitive assessments

	At-risk	bvFTD	PPA
ECAS (/136)	120.3 (6.3)	79.2 (30.3)	56.0 (32.1)
Language (/28)	26.9 (1.9)	24.3 (4.0)	15.9 (7.7)
Verbal Fluency (/24)	21.2 (2.5)	9.3 (7.8)	7.5 (7.7)
Executive function (/48)	42.3 (3.7)	27.5 (14.2)	20.4 (13.4)
Memory (/24)	18.0 (1.6)	8.8 (6.8)	6.0 (6.8)
Visuospatial (/12)	11.9 (0.3)	10.8 (2.4)	9.4 (3.9)
MMSE (/30)	28.4 (2.2)	24.4 (4.5)	18.0 (8.5)
MoCA (/30)	29.8 (6.9)	18.5 (6.4)	14.4 (7.8)
ACE-III (/100):	93.2 (6.6)	71.6 (18.8)	52.9 (27.8)

Table 2. Mean (standard deviation) scores on each of the cognitive assessments (and ECAS subscores)

	MMSE		MoCA		ACE-III	
	0	1	0	1	0	1
ECAS	0	11	2	7	6	10
	1	6	25	2	29	1

Table 3. Proportion of individuals who scored above (0)/below (1) the cut-offs on ECAS compared with other tests

Results

Comparison of ECAS subscores with neuropsychometric tests

Correlations were seen between the subscores and tests as follows (Table 4):

- Language:** BPVS, GNT, CPAL, D-KEFS Color-Word Interference Test
- Verbal fluency (VF):** all tests except VOSP Object Decision
- Executive function (EF):** D-KEFS Color-Word Interference Test, RMT Words, RMT Faces, CPAL, BPVS, GNT, WASI Block Design
- Memory:** RMT Words, RMT Faces, CPAL, BPVS, GNT
- Visuospatial skills (VS):** WASI Block Design, RMT Words, RMT Faces, CPAL, BPVS and GNT

	Language	VF	EF	Memory	VS
BPVS	rs= 0.437 p= 0.026*	rs= 0.710 p< 0.001***	rs= 0.555 p= 0.003**	rs= 0.617 p= 0.001***	rs= 0.479 p= 0.013**
GNT	rs= 0.547 p= 0.004**	rs= 0.816 p< 0.001***	rs= 0.708 p= 0.012*	rs= 0.797 p= 0.001***	rs= 0.532 p= 0.005*
D-KEFS Color-Word	rs= 0.414 p= 0.035*	rs= 0.487 p= 0.012*	rs= 0.487 p= 0.012*	rs= 0.459 p= 0.018*	rs= 0.206 p= 0.313
TMT Part B	rs= 0.2 p= 0.327	rs= 0.394 p= 0.047*	rs= 0.310 p= 0.124	rs= 0.342 p= 0.087	rs= 0.092 p= 0.655
RMT Faces	rs= 0.327 p= 0.103	rs= 0.585 p= 0.002**	rs= 0.461 p= 0.018*	rs= 0.463 p= 0.026*	rs= 0.584 p= 0.002**
RMT Words	rs= 0.286 p= 0.157	rs= 0.604 p= 0.001***	rs= 0.466 p= 0.017*	rs= 0.464 p= 0.017*	rs= 0.468 p= 0.016*
CPAL	rs= 0.406 p= 0.04*	rs= 0.574 p= 0.002*	rs= 0.611 p= 0.001***	rs= 0.504 p= 0.009**	rs= 0.487 p= 0.01**
WASI Block Design	rs= 0.254 p= 0.21	rs= 0.404 p= 0.041*	rs= 0.413 p= 0.036*	rs= 0.361 p= 0.070	rs= 0.390 p= 0.049*
VOSP Object Decision	rs= 0.077 p= 0.709	rs= 0.346 p= 0.083	rs= 0.196 p= 0.338	rs= 0.249 p= 0.220	rs= 0.334 p= 0.095

Table 4. Spearman's correlation coefficient (rs) results comparing ECAS subscores with psychometry, p values significant at alpha level (two-tailed) of * 0.05, ** 0.01, *** 0.001

VBM analysis of ECAS subscores

Distinct grey matter correlates were seen for each ECAS subscore:

- Language:** left temporal lobe (Figure 1B)
- Verbal Fluency:** dorsolateral prefrontal cortex and left anterior temporal lobe (Figure 1D)
- Executive Function:** left anterior and medial temporal lobe, dorsolateral prefrontal cortex and orbitofrontal cortex (Figure 1A)
- Memory:** left medial temporal lobe and bilateral anterior temporal lobes (Figure 1C)
- Visuospatial skills:** right parietal lobe and anterior cingulate (Figure 1E)

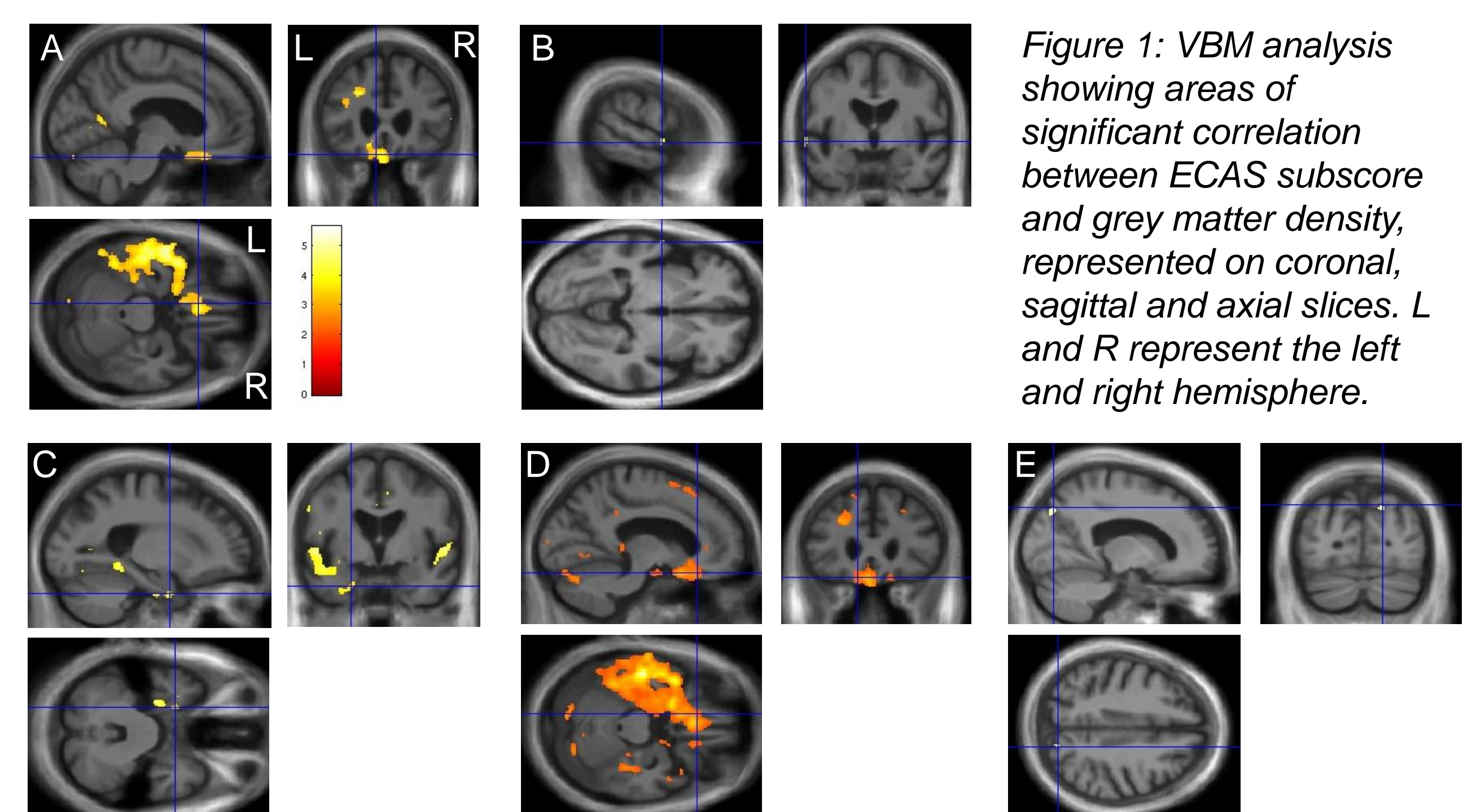


Figure 1: VBM analysis showing areas of significant correlation between ECAS subscores and grey matter density, represented on coronal, sagittal and axial slices. L and R represent the left and right hemisphere.

Conclusions

Overall, the ECAS is an effective tool for detecting cognitive impairment in FTD but has no better diagnostic accuracy than other more established tests. ECAS subscores correlate with formal psychometric tests within the same cognitive domain but are also highly correlated with performance in other domains. Similarly, neural correlates are consistent with known neuroanatomical areas involved in each domain but in some cases with a wider area than expected.

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