Clinical and neuropsychological features of behavioral variant frontotemporal dementia and phenocopy syndrome

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Introduction: The core features of **behavioural frontotemporal dementia (bvFTD)** (Rascovsky, 2011) are early behavioral and executive deficits, with insidious changes in personality and behaviour, often occurring in the absence of cognitive impairment **[Figure 1].** Some individuals who meet diagnostic criteria for bvFTD have a very slow disease course (over decades) with slow progression of cognitive impairment and normal MRI and positron emission tomography (PET) studies. They are classified as having **bvFTD phenocopy syndrome (bvFTD-PS)**. Considering that clinical symptoms and cognitive impairment may overlap in bvFTD and in bvFTD-PS (Kipps, 2010), a great attention has been recently focused on the differences obtained with a clinical and cognitive assessment.

Figure 1.
Diagnostic criteria for bvFTD proposed by Rascovsky et al. (2011) (from Lanata et al. 2015)

Possible bvFTD	Three or more of the following 6 features: ► Early behavioural disinhibition ► Early apathy or inertia ► Early loss of sympathy or empathy ► Early perseverative, stereotyped or compulsive/ritualistic behaviours ► Hyperorality and dietary changes ► Deficits in executive function with relative sparing of episodic memory and visuospatial skills (as determined by structured neuropsychological testing)
Probable bvFTD	Possible bvFTD AND evidence of BOTH the following: ► Significant functional decline ► Frontal and/or anterior temporal lobe atrophy on MRI or CT, or frontal and/or temporal hypoperfusion or hypometabolism on PET or SPECT
Definite bvFTD	Possible OR probable bvFTD AND evidence of EITHER of the following: ► Histopathological changes consistent with FTLD on biopsy or autopsy ► Presence of known FTLD pathogenic genetic mutation

Aim: To study the clinical and cognitive variables differentiating **bvFTD** patients and **bvFTD-PS**.

Matherials and methods: 33 patients (13 men and 20 women, mean age 65.3 ±9.4 years, mean disease duration 4 ±4.0 years) with a diagnosis of possible bvFTD according to Raskovsky criteria were recruited in the study. Each patient underwent a full neurological evaluation and an **extensive cognitive battery**. Behavioural assessments using the Neuropsychiatric Inventory **(NPI)** and the Repetitive Behaviours Subscale **(RBS)** were administrated. Clinical, demographic and cognitive data was analyzed with the Statistical Package for Social Science (SPSS 21.0) using t-test with Bonferroni correction and $\chi 2$ for categorical variables (p=0.05).

Results: bvFTD patients were younger than bvFTD-PS patients (p=0.009) **[Table 1].** Total NPI and RBS scores were similar in the two groups. However, in bvFTD **NPI-apathy** score and **eating/dietary changes** score were higher (p=0.005 and p=0.008 respectively) than in bvFTD-PS, while in bvFTD-PS **NPI-anxiety** score was greater (p=0.034). In the RBS scale subitems, **obsessive counting** was more frequent and severe in bvFTD (p=0.05). As for cognitive differences, although the MMSE score was similar, a more impaired **semantic and phonemic fluency** (phonemic: p=0.005; semantic: p=0.010), as well as deficit of working memory (**immediate prose memory test**: p=0.002) were detected in the bvFTD group **[Table 3].**

Table 1.
Demographic features of study population subdivided in bvFTD group and bvFTD-PS group. Age at the study, age at onset and disease duration are expressed in years (yr.); MMSE score is indicated as raw score (r.s.).

Demographic data	bvFTD n=19	bvFTD-PS n=11	p=
Mean age (yr.)	62.6 ±8.4	70.5 ±6.7	0.009
Gender M/F (% female)	8/11 (57.9%)	5/6 (54.5%)	0.858
Age at onset (yr.)	58.9 ±9.3	66.2 ±7.1	0.024
Disease duration (yr.)	3.7 ±3.8	4.4 ±4.2	0.688
MMSE score (r.s.)	21.4 ±5.8	22.9 ±5.8	0.489

Table 2.
Clinical features at disease onset in the two populations.

Clinical features (disease onset)	bvFTD n=19	bvFTD-PS n=11	p=
Positive family history	8 (42.1%)	3 (27.3%)	0.416
Behavioural symptoms at disease onset			
disinhibition	5 (26.3%)	7 (63.6%)	**0.044**
apathy	6 (31.6%)	0	**0.037**
OCD symptoms	4 (21.0%)	0	0.102
decreased speech output	3 (15.8%)	0	0.164
psychosis	1 (5.3%)	3 (18.2%)	0.255
cognitive executive deficits	1 (5.3%)	3 (18.2%)	0.255
Motor symptoms at disease onset	5 (26.3%)	4 (36.4%)	0.562

Table 3.
Summary of the neuropsychological battery in the two groups. RAVLT: Rey Auditory Verbal Learning Test; TMT: Trail Making Test; FAB: Frontal Assessment Battery; ROCF: Rey–Osterrieth complex figure.

Neuropsychological assessment	bvFTD n=15 (78.9%) mean raw score ±SD	bvFTD-PS n=9 (81.8%) mean raw score ±SD	p=
Demographic feature			
Age (yr.)	62.5 ±8.6	70.6 ±6.7	0.020
Gender (M/F) (female %)	7/8 (42.1%)	5/4 (36.4%)	0.673
Education (yr.)	10.3 ±4.7	7.9 ±2.8	0.130
MMSE	22.9 ±3.6	24.7 ±4	0.286
Digit Span Forward	4.4 ±1.1	4.4 ±2.4	0.976
Digit Span Backward	3.2 ±1.4	2.3 ±1.3	0.147
Immediate Prose Memory	4.6 ±3.3	9.7 ±2.3	**0.002**
Delayed Prose Memory	5.7 ±4.6	9.7 ±3.4	**0.053**
RAVLT Immediate Recall	24.1 ±9.9	32.0 ±12.9	0.324
RAVLT Delayed Recall	3.7 ±2.9	6.3 ±2.6	0.162
Attentional Matrix	37.2 ±13.0	42.4 ±12.1	0.348
TMT A *time*	103.6 ±81.1	81.6 ±40.2	0.395
TMT B *time*	227.6 ±161.7	267.0 ±147.1	0.630
FAB	10.3 ±4.1	12.5 ±1.3	0.152
Clock Test	9.6 ±7.5	5.2 ±3.7	0.173
Phonemic Fluency	12.5 ±10.7	26.1 ±9.1	**0.005**
Semantic Fluency	18.7 ±10.6	33.5 ±11.6	**0.010**
ROCF Copy	27.4 ±7.9	24.5 ±10.7	0.570
ROCF Recall	3.5 ±4.3	12.6 ±7.4	0.085

Conclusion: Patients with **bvFTD** were **more apathethic and less anxious** respect to bvFTD-PS patients. **Dietary/eating changes** may be specific markers of bvFTD, while disinhibition, lack of empathy and stereotypes are shared features of the two groups. **Working memory** e **verbal fluency deficits** could be cognitive variables associated more to bvFTD than its phenocopy.

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