

Sex differences in brain metabolism and neuropsychological profiles in behavioral variant frontotemporal dementia

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Objectives

This study investigated sex-related differences in neuropsychological profiles and brain metabolic patterns among patients diagnosed with the behavioral variant of frontotemporal dementia (bvFTD).

Materials and methods

All patients diagnosed with bvFTD underwent comprehensive neuropsychological evaluations. Brain metabolism was assessed through [¹⁸F]FDG-PET imaging and analyzed using statistical parametric mapping against a large control dataset (1).

NEUROPSYCHOLOGICAL ASSESSMENT – BASELINE

TEST (mean ± SD)	NORMAL RANGE	F GROUP	M GROUP	p-value
MMSE	≥ 24	23,69 ± 5,19	26,12 ± 4,34	0,248
MoCA	≥ 26	13,68 ± 6,13	17,73 ± 7,00	0,384
NPI		21,18 ± 18,29	43,00 ± 19,91	0,038

NEUROPSYCHOLOGICAL ASSESSMENT – FOLLOW-UP

TEST	NORMAL RANGE	F GROUP	M GROUP	p-value
MMSE	≥ 24	21,98 ± 5,79	22,14 ± 3,38	0,948
INDEX OF PROGRESSION		-1,22 ± 1,97	-3,64 ± 2,66	0,041
FAB	> 13,5	12,63 ± 1,26	8,85 ± 1,63	0,059
VERBAL FLUENCY TEST	> 17,35	28,00 ± 6,06	16,67 ± 1,53	0,027
DIGIT SPAN BACKWARD		3,33 ± 0,58	2,00 ± 0,47	0,053
ROCF - DR		15,25 ± 3,89	1,38 ± 1,94	0,046

MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; NPI: Neuropsychiatric Inventory; FAB: Frontal Assessment Battery; ROCF: Rey-Osterrieth Complex Figure Test (IR: immediate recall - DR: delayed recall). All results are corrected for age and education.

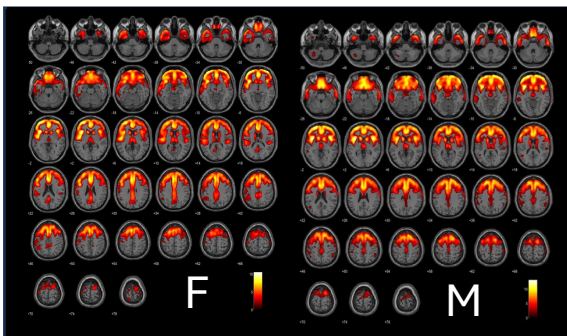


FIGURE 1: group-level [¹⁸F]-FDG-PET analysis in F-GROUP and M-GROUP vs healthy controls on axial sections.

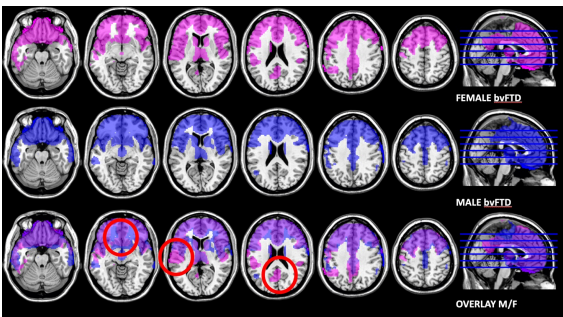


FIGURE 2: Comparative analysis of hypometabolism patterns between female and male groups.

Discussion and conclusions

Our findings suggest a potential sex-related divergence in bvFTD phenotype, with male patients demonstrating more prominent behavioral disturbances, steeper cognitive decline and wider metabolic dysfunction. Sex significantly influences both the clinical presentation and brain metabolic patterns in bvFTD. Only a few previous studies investigated differences in clinical presentation (2) and brain hypometabolism patterns (3) in FTD. Integrating sex as a biological variable in bvFTD research may improve diagnostic accuracy and promote the development of more tailored therapeutic strategies.

Results

Neuropsychological testing did not show significant differences at the baseline, but males showed a steeper cognitive decline (as shown by the index of progression, calculated by MMSE points loss per year - $p=0.041$), with a more severe language involvement ($p=0.027$), and executive functions ($p=0.059$) over disease course. Also, males exhibited more frequent and severe behavioral symptoms, as measured with NPI ($p=0.038$). [¹⁸F]FDG-PET imaging showed a shared pattern of frontal and temporal hypometabolism in both groups, though males exhibited more pronounced right-hemisphere involvement, with hypometabolism peaks observed in the right frontal operculum and right supramarginal gyrus.

TABLE 5: Clusters showing a statistically significant relative hypometabolism vs healthy controls

Group	pFWEc orr	MINI coordinates (atlas AAL)			ROI
		x	y	z	
F	0.000	-36	18	0	LI
	0.000	-32	58	-8	LAPFC
	0.000	-40	54	-6	LAPFC
M	0.000	-20	64	-4	LAPFC
	0.000	-34	18	-2	LI
	0.000	42	16	2	RFO
	0.000	52	-48	46	RSG
0.000	-48	-60	20	LAG	

HC: healthy controls; LI: left insula; LAPFC: left anterior prefrontal cortex; RFO: right frontal operculum; RSG: right supramarginal gyrus; LAG: left angular gyrus

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