

ADDITIONAL FILE 1

SUPPLEMENTARY MATERIALS

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Table S1. Clinical features and results of indicative biomarkers in the DLB group.

Variable	N=49
Clinical core feature, No. (%)	
Fluctuations	17 (34.7)
Visual hallucinations	29 (59.2)
REM sleep behavior disorder	23 (46.9)
Parkinsonism	45 (91.8)
1 out 4 clinical core features	9 (18.4)
2 out 4 clinical core features	21 (42.9)
3 out 4 clinical core features	13 (26.5)
4 of 4 clinical core features	6 (12.2)
Biomarker, No. of patients with positive finding/No. tested (%)	
DaTscan	25/29 (86.2)
¹²³ I-MIBG uptake at myocardial scintigraphy	10/11 (90.9)
REM sleep without atonia at PSG	10/14 (71.4)

Table S2. CSF NfL, GFAP and AD core biomarker values across diagnostic groups.

	FTD	PSP	CBS	DLB	AD	SNAP
n	59	31	29	49	97	51
NfL	2459 (1492-4676) ^{a-e}	1664 (1109-2086) ^f	1454 (1087-2481) ^c	1045 (789-1334)	1061 (863-1508)	1114 (676-2710)
GFAP	9118 (5613-14385)	10383 (8248-15379)	12817 (8269-18309)	10635 (6507-16309)	11917 (8515-17388)	9462 (5517-14541)
t-tau	269 (201-381) ^d	200 (154-284) ^d	309 (215-478) ^d	246 (170-251) ^d	640 (492-986) ^e	256 (182-353)
p-tau181	28 (23-36) ^{d,g}	30 (22-46) ^{d,g}	45 (31-81) ^{d-f}	31 (25-48) ^d	109 (82-153) ^e	31 (25-42)
A β 42/40	0.93 (0.82-0.99) ^{c,d}	0.86 (0.78-0.97) ^{d,f}	0.71 (0.56-0.94) ^{d,e}	0.84 (0.56-0.93) ^{d,e}	0.43 (0.39-0.49) ^e	0.94 (0.87-1.00)
A β 42	671 (533-671) ^d	585 (463-1016) ^d	578 (479-832)	607 (350-759) ^h	476 (369-592) ^e	778 (541-1000)
A β 40	7510 (5732-9344) ^d	7731 (5657-11387) ^d	9191 (7159-11207) ^j	7348 (6679-9506) ^d	11165 (8891-13670) ^e	8567 (6450-10729)

Biomarker values are expressed in pg/ml as median (IQR range). ^a vs. PSP ≤ 0.001 ; ^b vs. CBS ≤ 0.01 ; ^c vs. DLB ≤ 0.001 ; ^d vs. AD ≤ 0.001 ; ^eNfL FTD vs SNAP < 0.001 ; ^f vs. DLB ≤ 0.05 ; ^g vs. CBS ≤ 0.001 ; ^h vs. SNAP ≤ 0.01 ; ^j vs. AD ≤ 0.05 .

Table S3. Plasma NfL, GFAP and p-tau181 values across diagnostic groups.

	FTD	PSP	CBS	DLB	AD	SNAP	HC
n	59	31	29	49	97	51	60
NfL	44.9 (28.1-68.6) ^{a,f}	26.6 (18.5-36.0) ^f	24.5 (21.4-51.8) ^{f,g}	26.3 (15.9-38.2) ^f	21.9 (17.0-27.9) ^f	19.1 (12.6-28.7) ^f	10.1 (8.5-14.6)
GFAP	198.2 (143.9-316.8) ^{d,f}	235.2 (187.5-312.7) ^{d,f}	302.9 (211.2-428.2) ^{e,f}	293.6 (227.8-485.9) ^{e,f}	404.7 (279.7-503.0) ^{e,f}	177.4 (118.8-260.5) ^f	121.9 (91.2-156.3)
p-tau181	1.1 (0.7-1.6) ^d	1.0 (0.8-1.7) ^d	1.1 (0.9-2.1) ^d	1.5 (0.8-2.6) ^{d,f}	3.2 (2.4-4.3) ^{e,f}	1.2 (0.8-1.9)	1.0 (0.8-1.3)

Biomarker values are expressed in pg/ml as median (IQR range). ^a vs. PSP ≤ 0.001 ; ^b vs. CBS ≤ 0.001 ; ^c vs. DLB ≤ 0.001 ; ^d vs. AD ≤ 0.001 ; ^e vs. SNAP ≤ 0.001 ; ^f vs. HC ≤ 0.001 ; ^g vs. SNAP ≤ 0.01 .

Table S4. CSF and plasma NfL, GFAP and p-tau181 across FTD phenotypic continuum.

	<i>pure FTD</i>				<i>FTD plus</i>		
phenotype	All	BvFTD	nvPPA	lvPPA	All	FTD+park	FTD+ALS
n	43*	33	6	2	16	8	8
CSF							
NfL	2376 (1485-4405)	2150 (1389-4253)	4008 (2643-4872)	2190 (1920-2459)	3214 (1511-7063)	2776 (1660-6982)	4121 (1409-14846)
p-tau	28.0 (23.0-36.0)	27.0 (22.0-35.0)	33.5 (22.8-43.8)	38.0 (28.0-48.0)	29.0 (23.3-38.3)	26.0 (21.5-38.3)	31.0 (24.8-46.5)
GFAP	9351 (5594-16399)	8231 (5280-16052)	9759 (6350-15878)	-	5658 (4801-11577)	5939 (4862-7281)	5658 (3958-12180)
Plasma							
NfL	44.9 (26.7-64.3)	42.6 (26.5-66.2)	54.8 (25.2-67.3)	26.8 (16.6-37.0)	49.9 (34.3-113.1)	59.8 (43.0-96.9)	41.2 (29.2-292.6)
p-tau	1.0 (0.7-1.5)	1.0 (0.7-1.4)	0.9 (0.6-1.6)	0.9 (0.8-1.1)	1.3 (0.6-1.7)	1.2 (0.7-1.6)	1.3 (0.6-1.9)
GFAP	189.5 (130.9-273.0)	169.5 (134.5-282.4)	158.2 (120.8-219.3)	144.0 (102.1-185.9)	295.9 (180.5-337.5)	319.3 (263.5-365.8)	192.3 (160.0-326.5)

Biomarker values are expressed in pg/ml as median (IQR range). *Includes 2 cases with mixed BvFTD/PPA features.

Table S5. CSF and plasma NfL, GFAP and p-tau181 in genetic and sporadic FTD.

	genetic [#]				sporadic [#]
mutation	<i>C9orf72</i>	<i>GRN</i>	Others	All	
n	7	6	5	18	41
CSF					
NfL	4498 (1492-4844)	5604 (3910-7394)	3565 (1490-8153)	4502 (2085-6409) ^a	2150 (1390-3800)
p-tau	42 (16-51)	25 (20-28)	35 (28-42)	28 (22-43)	28 (23-34)
GFAP	9759 (5432-12180)	14121 (9332-31687)	8231 (5539-17150)	10690 (7346-16948)	6865 (5096-12723)
Plasma					
NfL	42.8 (28.1-69.1)	72.6 (63.9-79.4)	39.6 (17.1-84.8)	57.2 (30.5-76.1)	43.6 (26.9-64.3)
p-tau	1.4 (0.6-1.7)	0.9 (0.6-1.2)	0.7 (0.3-2.4)	0.9 (0.6-1.7)	1.1 (0.8-1.6)
GFAP	153.8 (132.6-187.7) ^b	284.9 (216.5-384.6) ^c	129.5 (91.4-240.7)	182.6 (130.9-273.0)	199.0 (150.4-324.3)

Biomarker values are expressed in pg/ml as median (IQR range). ^a vs. sporadic ≤ 0.05 ; ^b vs. genetic *GRN* ≤ 0.05 ; ^c vs. genetic Others ≤ 0.05 . [#]The FTD-ALS phenotype was slightly more frequent in the genetic (22.2%) than sporadic group (9.7%).

Fig. S1. Plasma NfL levels in the SNAP group according with the clinical presentation.

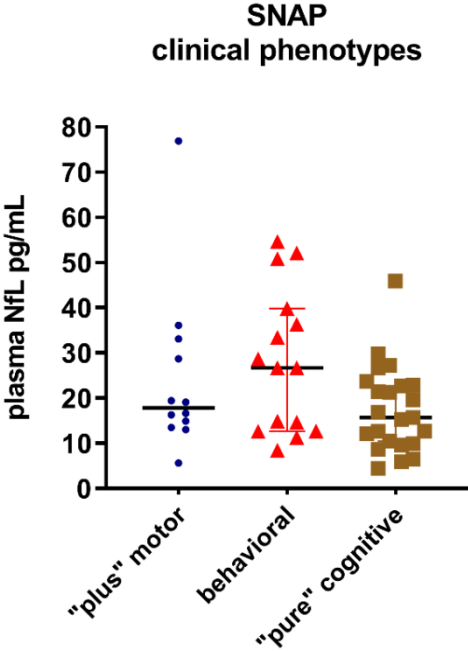


Fig. S2. Accuracy of plasma NfL, p-tau181 and GFAP in discriminating between healthy controls and disease groups.

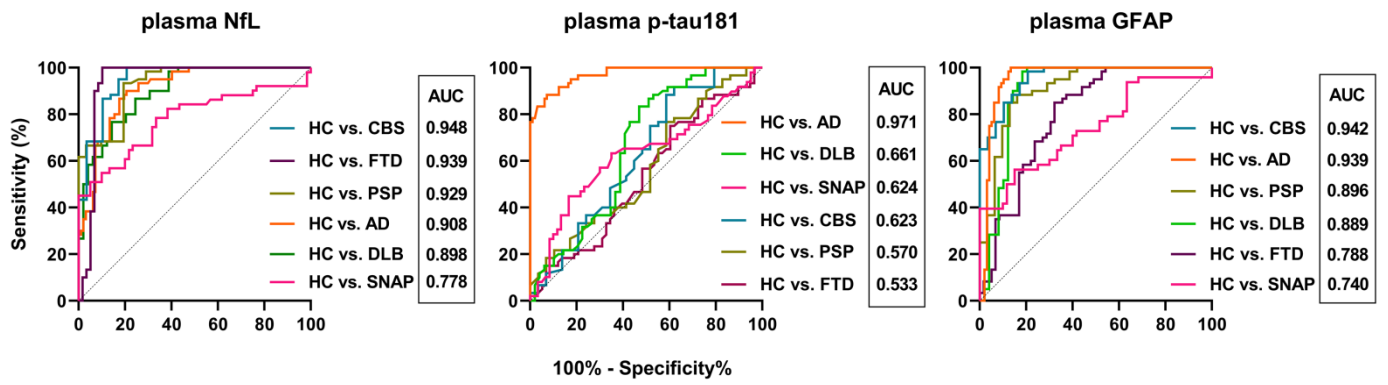
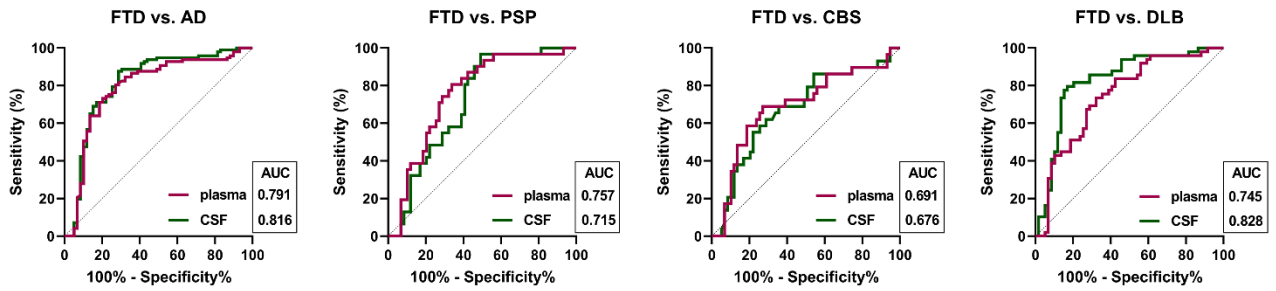
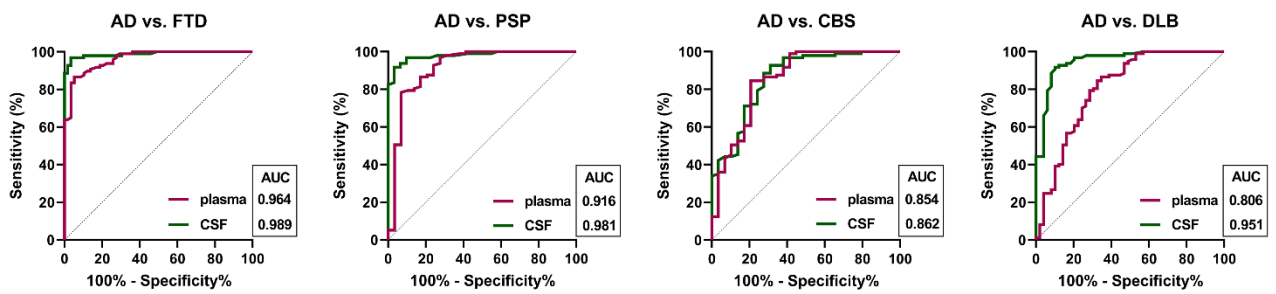


Fig. S3. Comparisons between CSF and plasma accuracy for each biomarker across disease groups.

NfL



p-tau181



GFAP

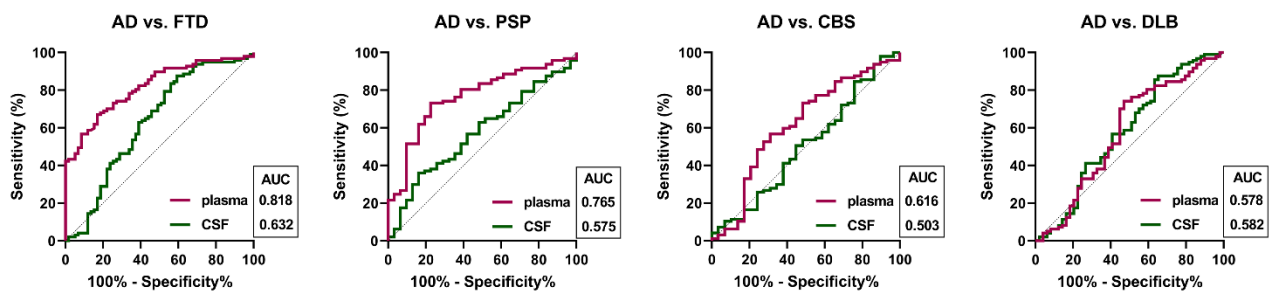


Fig. S4. Plasma biomarker levels in CBS and DLB according with the amyloid status (left) and ROC curves after excluding A+ cases in non-AD disease groups (right).

