Table e-1. Differences of CSF NfL between the patient and control groups

	bvFTD	FTD-MND	svPPA	nfvPPA	lvPPA	CBS	PSP
Controls	2194	18258	2177	1371	757	1690	933
p-value	<0.001	<0.001	<0.001	<0.001	0.97	<0.001	<0.001
bvFTD		16064	-17	-823	-1437	-504	-1261
p-value		<0.001	1.00	1.00	0.98	1.00	0.002
FTD-MND			-16081	-16887	-17501	-16568	-17325
p-value			<0.001	<0.001	<0.001	<0.001	<0.001
svPPA				-805	-1419	-487	-1244
p-value				1.00	0.99	1.00	0.10
nfvPPA					-614	319	-439
p-value					1.00	1.00	1.00
lvPPA						933	175
p-value						1.00	1.00
CBS							-757
p-value							0.61

Differences between medians are displayed (column minus row). Significances (corrected for multiple comparisons) of the ANCOVA analysis with correction for age are displayed.

bvFTD: behavioral variant FTD; CBS: corticobasal syndrome; CSF: cerebrospinal fluid; FTD: frontotemporal dementia; FTD-MND: FTD with concomitant motor neuron disease; lvPPA: logopenic variant PPA; NfL: neurofilament light chain; nfvPPA: non-fluent variant PPA; PPA: primary progressive aphasia; PSP: progressive supranuclear palsy; svPPA: semantic variant PPA

Table e-2. Differences of CSF p/t-tau ratio between the patient and control groups

	bvFTD	FTD-MND	svPPA	nfvPPA	lvPPA	CBS	PSP
Controls	-0,052	-0,089	-0,057	-0,033	-0,043	-0,044	-0,026
p-value	<0.001	<0.001	<0.001	0.003	0.17	<0.001	<0.001
bvFTD		-0,037	-0,005	0,019	0,009	0,008	0,026
p-value		<0.001	1.0	0.75	1.0	0.95	0.001
FTD-MND			0,032	0,056	0,046	0,045	0,063
p-value			<0.001	<0.001	0.16	<0.001	<0.001
svPPA				0,024	0,014	0,013	0,031
p-value				0.91	1.0	1.0	0.054
nfvPPA					-0,010	-0,010	0,007
p-value					1.0	1.0	1.0
lvPPA						-0,001	0,017
p-value						1.0	1.0
CBS							0,017
p-value							0.89

Differences between medians are displayed (column minus row). Significances (corrected for multiple comparisons) of the ANCOVA analysis with correction for age are displayed.

bvFTD: behavioral variant FTD; CBS: corticobasal syndrome; CSF: cerebrospinal fluid; FTD: frontotemporal dementia; FTD-MND: FTD with concomitant motor neuron disease; lvPPA: logopenic

variant PPA; NfL: neurofilament light chain; nfvPPA: non-fluent variant PPA; PPA: primary progressive aphasia; PSP: progressive supranuclear palsy; svPPA: semantic variant PPA

Table e-3. Diagnostic performance of CSF NfL, p/t-tau ratio and the combination

	AUC	95% CI AUC	*p*-value	Cut-off	Sensitivity	Specificity	NPV	PPV
Case vs control								
NfL	0.87	0.81-0.92	<0.001	≥1613	78.5%	88.9%	35.7%	98.1%
p/t-tau ratio	0.86	0.83-0.90	<0.001	≤0.153	73.3%	93.3%	30.9%	98.9%
Combined	0.91	0.88-0.95	<0.001	≥0.860	79.8%	93.3%	38.9%	98.9%
FTLD-TDP vs FTLD-tau								
NfL	0.59	0.45-0.73	0.26	n.s.	n.s.	n.s.	n.s.	n.s.
p/t-tau ratio	0.73	0.60-0.87	0.005	≤0.121	66.7%	76.5%	44.8%	88.9%
Combined	0.75	0.62-0.88	0.004	≤0.212	59.1%	87.5%	43.8%	92.9%

Diagnostic performance per application and per biomarker or combination. To discriminate cases from controls, the combination outperformed NfL (p=0.04 compared to AUC of combination) and the ratio (p<0.01) alone. To discriminate TDP from tau pathology, the ratio performed similar to the combination of NfL and the ratio (p=0.95).

AUC: area under the curve from the receiver operating curve analysis; CI: confidence interval; CSF: cerebrospinal fluid; FTLD-tau: frontotemporal lobar degeneration with tau inclusions; FTLD-TDP: frontotemporal lobar degeneration with TAR DNA-binding protein 43 inclusions; NfL: neurofilament light chain; NPV: negative predictive value; n.s.: not significant; PPV: positive predictive value.

Table e-4. Association of NfL and p/t-tau ratio with demographic and clinical variables.

	NfL			p/t-tau ratio		
	r_s	*n*	*p*-value	r_s	*n*	*p*-value
Age at CSF collection	-0.03	335	0.65	0.12	352	0.03
Sex	n/a	335	0.38	n/a	352	0.53
Disease duration at CSF collection	-0.22	335	<0.001[a]	0.15	352	0.006[b]
Genetic status[c]	n/a	334	0.001[c]	n/a	351	0.005[c]
MMSE	-0.15	273	0.01[d]	0.10	291	0.08
FAB	-0.15	201	0.03[a]	0.12	219	0.07
CDR	0.08	208	0.25	-0.08	227	0.25
CDR-SB	0.38	51	0.005[a]	-0.31	51	0.03[a]

All clinical patients and no controls were included in the correlation analysis. For the cognitive scales, only assessments within 6 months of CSF collection were considered.

[a]After stratification on clinical diagnosis, an association was confirmed in bvFTD. [b]Stratification by clinical diagnosis did not yield an association. [c]The following groups were compared: patients with a mutation in *GRN*, *C9orf72*, *MAPT*, and patients without a known mutation, one patient with a *optineurin* mutation was excluded; post-hoc analysis showed higher NfL levels and lower p/t-tau ratios in *GRN* mutations than in those without a known mutation. [d]After stratification on clinical diagnosis, an association was confirmed in CBS.

bvFTD: behavioral variant frontotemporal dementia; CBS: corticobasal syndrome; CDR: clinical dementia rating scale; CDR-SB: clinical dementia rating scale sum of boxes; CSF: cerebrospinal fluid; FAB: frontal assessment battery; MMSE: Mini-Mental State Examination; n/a: not applicable; NfL: neurofilament light chain; r_s: Spearman's correlation coefficient.