Supplementary material – CSF assay methodology

Total tau (T-tau), phosphorylated tau (P-tau) and β-amyloid 1-42 (Aβ1-42) were analyzed using INNOTEST enzyme-linked immunosorbent assays (ELISAs (Fujirebio Europe N.V., Gent, Belgium). Other markers of amyloid processing were measured using the MSD Aβ Triplex assay (Meso Scale Discovery, Rockville, MD), a multiplexed method in which C-terminally specific antibodies are used selectively to capture Aβ forms ending at amino acids 38, 40 and 42, respectively, which are then quantified using the 6E10 detector antibody. This assay is thus not specific to the 1st amino acid of the Aβ peptides (the epitope of 6E10 lies within amino acids 3 to 8 in the Aβ sequence) and the measured Aβ isoforms are therefore called AβX-38, AβX-40 and AβX-42. Neurofilament light chain (NFL) concentrations were determined using the NF-light method (UmanDiagnostics, Umeå Sweden); YKL-40, also known as chitinase-3-like protein 1 (CHI3L1), was measured using the Human Chitinase 3-like 1 Quantikine ELISA Kit (R&D systems, Minneapolis, MN). Amyloid precursor protein soluble metabolites α and β (sAPPα, sAPPβ) were measured using a commercial duplex immunoassay with electrochemiluminescence detection (Meso Scale Discovery, Rockville, MD). Inter-plate co-efficients of variation for internal standards (pooled AD CSF) were: YKL-40: 9.59 %; NFL: 7.72%; sAPPα: 23.03%; sAPPβ: 28.56%; AβX-38: 5.52%; AβX-40: 7.57%; AβX-42: 10.17%.

Supplementary Table S1 Diagnostic accuracy of Aβ1-42, T-tau, T-tau/Aβ1-42 ratio, P-tau and AβX-42/X-40 ratio in test and validation cohorts based on pre-LP diagnostic classification and diagnostic accuracy in the pathologically or genetically defined sub-cohort. AD: Alzheimer's disease; DLB: dementia with Lewy bodies; bvFTD: behavioural variant frontotemporal dementia; PNFA: progressive non-fluent aphasia; SD: Semantic dementia; HC: healthy control.

		Test cohort (used to estimate the cut-point)(data from tables 3 and 4) (n=275)		**Validation cohort (using test cohort cut-point) (n=143)**		**Pathologically or genetically confirmed sub-cohort (n=26)**	
Diagnostic Groups compared	**Biomarker**	**Optimal cut-point at 85% sensitivity**	**Specificity**	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
AD vs HC	AβX-42/X-40	<0.060	93%	82%	80%		
	Aβ1-42 (pg/mL)	<529.0	90%	71%	80%		
	T-tau/Aβ1-42	>0.64	83%	88%	89%		
	T-tau (pg/mL)	>312.0	53%	87%	78%		
	P-tau (pg/L)	>48.9	54%	83%	78%		
AD vs non-AD dementia	T-tau/Aβ1-42	>0.64	56%	88%	76%	100%	60%
	AβX-42/X-40	<0.060	68%	82%	74%	92%	100%
	T-tau (pg/mL)	>312.0	51%	87%	53%	94%	60%
	P-tau (pg/L)	>48.9	41%	83%	70%	83%	43%
	Aβ1-42 (pg/mL)	<529.0	48%	71%	77%	88%	60%
AD vs all (inc. HC)	T-tau/Aβ1-42	>0.64	63%	88%	76%		
	AβX-42/X-40	<0.060	76%	83%	74%		
	T-tau (pg/mL)	>312.0	51%	87%	50%		
	Aβ1-42 (pg/mL)	<529.0	59%	71%	77%		

	P-tau (pg/L)	>48.9	45%	83%	70%		