SUPPLEMENTARY DATA

Table S1. Results of the Linear Regression Analyses Relating CSF Biomarker Levels to Cognitive Domain Scores.

Independent Variable	Dependent Variable	Univariable Linear Regression		Multivariable Linear Regression*	
		sβ (95% CI)	p	sβ (95% CI)	p
CSF t−α−syn (pg/mL)	Memory	−0.277 (−0.810–0.201)	0.223	−0.154 (−0.672–0.335)	0.488
	Attention	−0.085 (−0.561–0.392)	0.715	0.143 (−0.278–0.562)	0.484
	Executive function	−0.189 (−0.687–0.293)	0.411	−0.079 (−0.497–0.333)	0.680
	Visuospatial function	−0.360 (−0.864–0.107)	0.119	−0.146 (−0.652–0.344)	0.520
	Language	−0.325 (−0.864–0.169)	0.174	−0.198 (−0.787–0.364)	0.443
CSF p−α−syn (pg/mL)	Memory	0.061 (−0.557–0.720)	0.793	−0.018 (−0.608–0.559)	0.930
	Attention	−0.043 (−0.521–0.435)	0.853	−0.134 (−0.528–0.261)	0.483
	Executive function	0.479 (0.060–0.936)	0.028	0.411 (0.108–0.747)	0.012
	Visuospatial function	−0.035 (−0.574–0.499)	0.885	−0.095 (−0.583–0.376)	0.652
	Language	−0.143 (−0.690–0.386)	0.559	−0.182 (−0.735–0.347)	0.455
CSF p−α−syn/t−α−syn	Memory	0.141 (−0.367–0.676)	0.542	−0.005 (−0.516–0.506)	0.983
	Attention	−0.044 (−0.521–0.434)	0.851	−0.259 (−0.662–0.146)	0.195
	Executive function	0.479 (0.060–0.937)	0.028	0.402 (0.065–0.771)	0.023
	Visuospatial function	0.249 (−0.247–0.779)	0.291	0.069 (−0.428–0.577)	0.757
	Language	0.154 (−0.370–0.695)	0.529	0.012 (−0.561–0.586)	0.963
CSF NfL (pg/mL)	Memory	−0.667 (−1.059–0.308)	0.001	−0.588 (−0.938–0.268)	0.002
	Attention	−0.357 (−0.852–0.110)	0.122	−0.316 (−0.741–0.094)	0.119
	Executive function	−0.461 (−0.992–0.026)	0.041	−0.347 (−0.780–0.013)	0.059
	Visuospatial function	−0.136 (−0.670–0.389)	0.578	−0.024 (−0.529–0.475)	0.916
	Language	0.004 (−0.497–0.507)	0.986	0.160 (−0 324–0.637)	0.491
CSF Aβ42 (ng/mL)	Memory	0.321 (−0.078–0.721)	0.110	0.110 (−0.293–0.513)	0.577
	Attention	0.483 (0.113–0.851)	0.012	0.354 (0.012–0.697)	0.043
	Executive function	0.446 (0.070–0.823)	0.022	0.200 (−0.155–0.554)	0.253
	Visuospatial function	0.123 (−0.338–0.611)	0.558	0.079 (−0.342–0.518)	0.674
	Language	−0.014 (−0.510–0.480)	0.950	−0.049 (−0.543–0.435)	0.820
CSF t−tau (ng/L)	Memory	−0.211 (−0.623–0.200)	0.301	−0.128 (−0.526–0.269)	0.511
	Attention	−0.055 (−0.476–0.366)	0.790	0.145 (−0.223–0.513)	0.422
	Executive function	−0.179 (−0.593–0.236)	0.382	−0.119 (−0.476–0.238)	0.496
	Visuospatial function	−0.404 (−0.786–0.009)	0.045	−0.179 (−0.575–0.223)	0.368
	Language	−0.312 (−0.807–0.129)	0.147	−0.184 (−0.695–0.296)	0.409
CSF p−tau (ng/L)	Memory	−0.270 (−0.676–0.135)	0.181	−0.156 (−0.548–0.235)	0.415
	Attention	−0.163 (−0.579–0.253)	0.426	0.052 (−0.317–0.421)	0.773
	Executive function	−0.342 (−0.738–0.054)	0.087	−0.255 (−0.593–0.083)	0.132
	Visuospatial function	−0.424 (−0.813–0.033)	0.035	−0.243 (−0.626–0.140)	0.201
	Language	−0.396 (−0.993–0.026)	0.062	−0.329 (−0.916–0.113)	0.119

sβ =standardized regression coefficient * including the variables age, gender, and level of education. Abbreviations: CSF, cerebrospinal fluid; t−α−syn, total α−synuclein; p−α−syn, phosphorylated α−synuclein; NfL, neurofilament light chain; Aβ42, amyloid−β42; t−tau, total tau; p−tau, phosphorylated tau.

Table S2. Detailed Description of Neuropsychological Tests and Outcome Measures

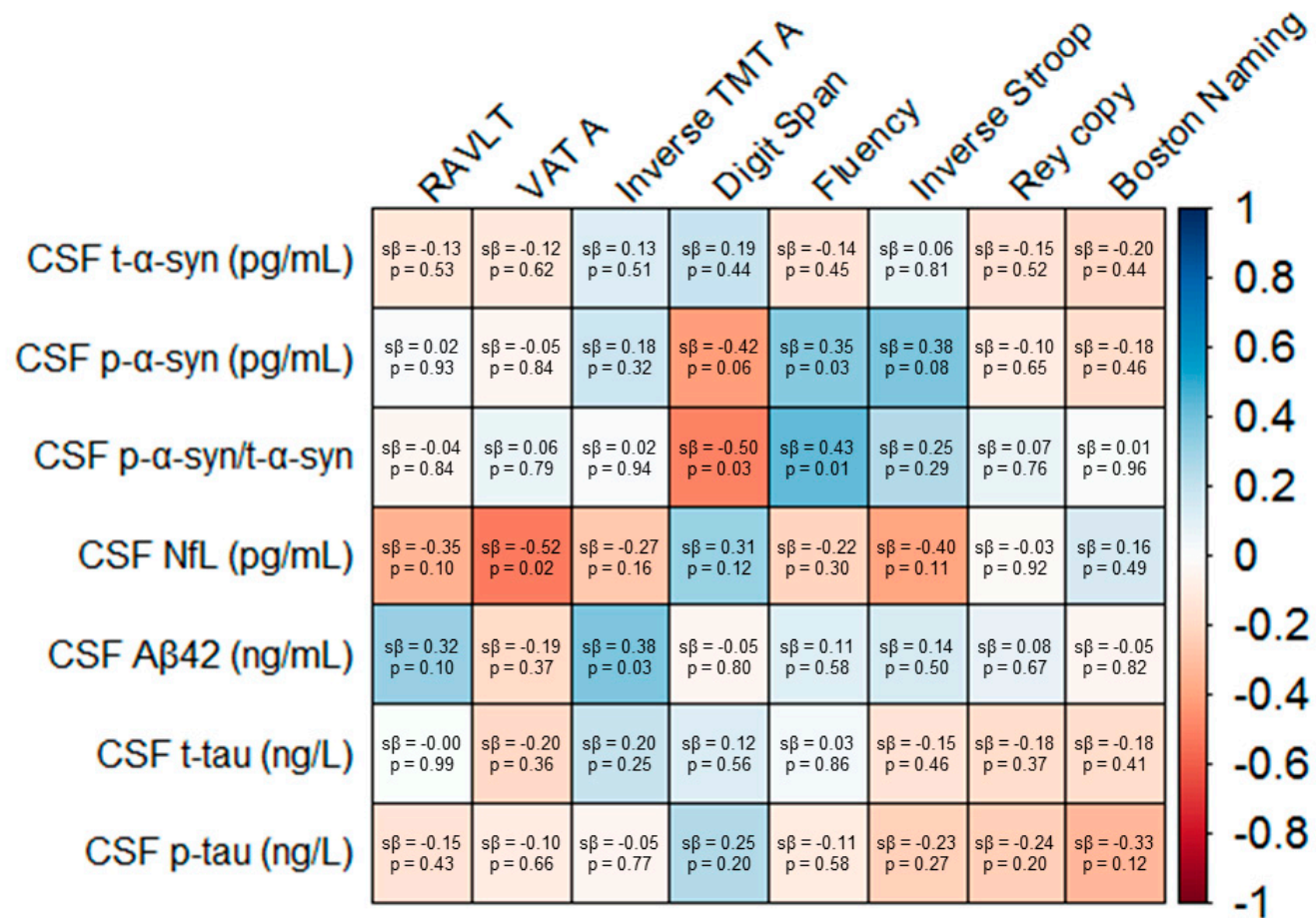| Neuropsychological Test	Test Variable Used	Cognitive Component	Description	Outcome Measure
Memory				
Rey Auditory Verbal Learning Test (RAVLT)	Delayed recall	Free recall	A list of 15 unrelated words are read to the subjects, repeated over 5 trials. After a delay of 20 min, subjects are asked to recall as many words as possible.	Number of words Range: 0–15
Visual Attention Test (VAT)	Part A trial 1	Automatic learning	Subjects are asked to recall unusual pairs of objects (e.g. a monkey with an umbrella).	Number of objects Range: 0–6
Attention				
Trail Making Test	Part A	Attention	Subjects are asked to connect ascending numbers as quickly as possible.	Time needed to complete (seconds)
WAIS–III Digit Span	Forward condition	Attention	Subjects are asked to recall series of numbers in a correct order.	Number of correct series Range: 0–21
Executive function				
Stroop Color Word interference test	Card 3/2	Mental set shifting/ response inhibition	Subjects need to name series of colors and words, which reflects processing speed (card 1 and 2). On card 3, names of words are printed in conflicting colors (e.g. red is printed in blue) and subjects need to name the color of the ink instead of the word.	Time needed on card 3 / time needed on card 2 (seconds)
Category Fluency	–	Working memory/ mental set shifting	Subjects are asked to produce as many animals as possible within a time span of 60 s.	Number of animals
Visuospatial function				
Rey Complex Figure	Copy	Visuospatial orientation Visuoconstruction	Subjects are asked to copy a complex figure. The figure consists of 18 elements.	Score based on drawn elements Range: 0–36
Language				
Boston Naming Test–short version A	–	Word retrieval	Subject are asked to name objects from 29 line drawings.	Score based on correctly named objects Range: 0–87

Figure S1. Associations of CSF biomarker levels with neuropsychological test scores. Data are standardized β coefficients from linear regression models, adjusted for age, gender, and level of education. Color intensity is based on the standardized β coefficients. Abbreviations: CSF, cerebrospinal fluid; t–α–syn, total α–synuclein; p–α–syn, phosphorylated α–synuclein; NfL, neurofilament light chain; Aβ42, amyloid–β42; t–tau, total tau; p–tau, phosphorylated tau; RAVLT, Rey Auditory Verbal Learning Test; VAT, Visual Association Test; TMT, Trail Making Test.

Table S3. Individual Levels of CSF Total α–synuclein and Phosphorylated α–synuclein in 21 Patients with Early–stage Parkinson's Disease

Subject	CSF t–α–syn (pg/mL)	CSF p–α–syn (pg/mL)	CSF p–α–syn/t–α–syn (%)
1	1436	274	19,1
2	723	243	33,6
3	1111	297	26,8
4	1323	198	15
5	1186	234	19,8
6	740	257	34,7
7	1551	178	11,5
8	1802	284	15,7
9	1416	268	18,9
10	1247	203	16,3
11	1401	354	25,2
12	1613	294	18,2
13	1217	209	17,2
14	1187	206	17,4
15	1225	275	22,4
16	1271	184	14,5
17	1950	165	8,5
18	1710	281	16,4
19	1263	309	24,5
20	1371	309	22,6
21	1205	321	26,6

Abbreviations: CSF, cerebrospinal fluid; t–α–syn, total α–synuclein; p–α–syn, phosphorylated α–synuclein.