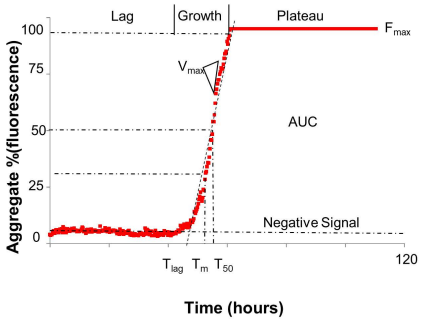
Supplementary Information

Supplementary figures

Supplementary Figure 1. The relative seeding activities of the CSF sample presented as plotting fluorescence readouts against assay time.

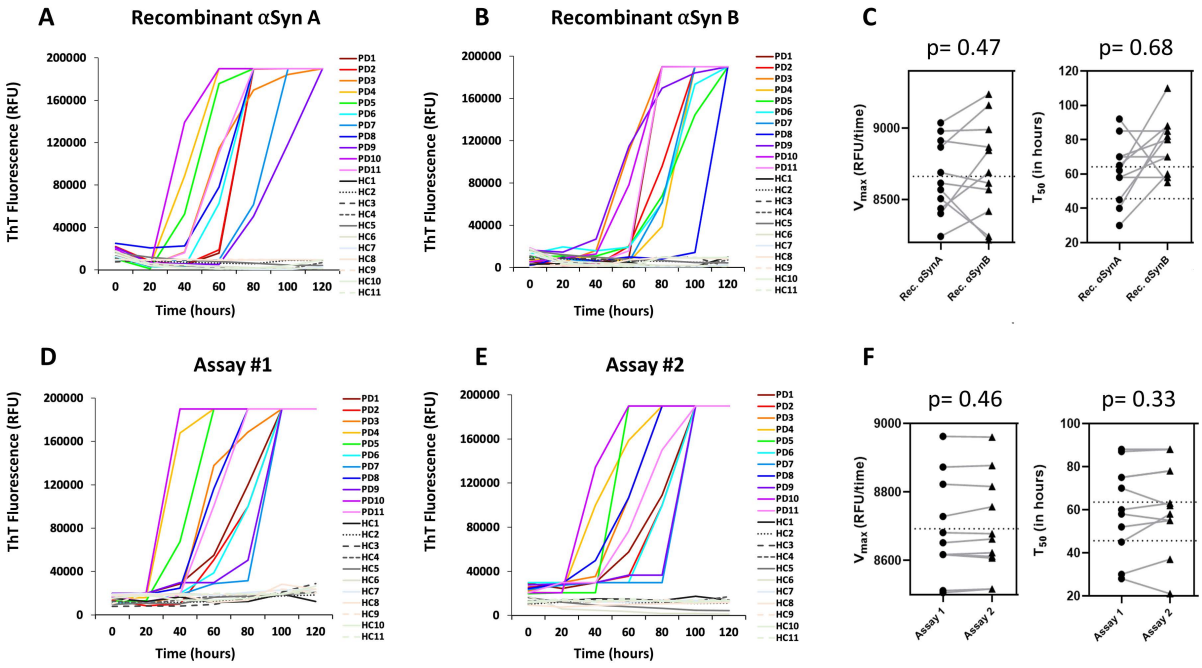
Lag phase (T_{lag}) = time each positive reaction exceeds the threshold (RFU>5 SD); Maximum fluorescence value (F_{max})= highest mean fluorescence value achieved; T_{50} = time latency to reach 50% of the F_{max}; Maximum slope (V_{max}) = maximum increase per unit of time; The area under curve (AUC).

Supplementary Fig. 1



Supplementary Figure 2. Impact of experimental conditions on RT-QuIC detection of seeding activity in CSF.

(A-C) Duplicate RT-QuIC seeding responses using two different batches of rec αSyn show similar sensitivity and specificity. (D-F) Independent experiments (Assay #1 and #2) showing the replicability of the RT-QuIC kinetics using the same batch of rec αSyn as a substrate. Traces represent the average Thioflavin T (ThT) fluorescence using CSF samples from Parkinson's disease (PD) patients and healthy controls (HC). Paired t-test was performed between different rec αSyn substrates (C) and two different assays (F).



Supplementary Tables

Supplementary table 1: Non-parametric associations between RT-QuIC parameters and clinical data for 74 Parkinson's disease patients. All data is estimate (95% confidence interval); p-value. Clinical data and RT-QuIC parameters are all standardised to unit standard deviation to aid interpretability. Spearman rank correlations, Rank sum or Fisher's exact test. For the rank sum test a negative z indicates that higher scores of that continuous variable are more likely to have a positive response to the binary variable.

Clinical data	RT-QuIC positive	T_{lag}	V_{max}	T_{50}	F_{max}	AUC
MDS-UPDRS I	z=1.49; p=0.14[a]	rho=0.22; p=0.066[b]	rho=-0.18; p=0.12[b]	rho=0.35; p=0.003[b] **	rho=-0.04; p=0.77[b]	rho=-0.18; p=0.13[b]
MDS-UPDRS II	z=0.95; p=0.34[a]	rho=0.07; p=0.53[b]	rho=-0.07; p=0.56[b]	rho=0.16; p=0.18[b]	rho=-0.04; p=0.73[b]	rho=-0.08; p=0.48[b]
MDS-UPDRS III	z=0.12; p=0.90[a]	rho=0.16; p=0.18[b]	rho=-0.07; p=0.53[b]	rho=0.19; p=0.11[b]	rho=-0.14; p=0.23[b]	rho=-0.11; p=0.37[b]
MDS-UPDRS IV	z=0.35; p=0.73[a]	rho=0.00; p=0.98[b]	rho=0.23; p=0.047[b] *	rho=0.08; p=0.51[b]	rho=0.12; p=0.31[b]	rho=-0.03; p=0.80[b]
MMSE	z=-0.75; p=0.45[a]	rho=-0.16; p=0.18[b]	rho=0.19; p=0.10[b]	rho=-0.18; p=0.12[b]	rho=0.19; p=0.11[b]	rho=0.04; p=0.75[b]
MoCA	z=-1.43; p=0.15[a]	rho=-0.21; p=0.066[b]	rho=0.11; p=0.37[b]	rho=-0.24; p=0.042[b] *	rho=0.06; p=0.61[b]	rho=0.05; p=0.66[b]
Age at lumbar puncture	z=-0.71; p=0.48[a]	rho=-0.05; p=0.70[b]	rho=0.10; p=0.41[b]	rho=-0.11; p=0.35[b]	rho=0.13; p=0.26[b]	rho=0.10; p=0.38[b]
Disease duration from diagnosis	z=0.71; p=0.48[a]	rho=-0.08; p=0.50[b]	rho=0.02; p=0.89[b]	rho=-0.05; p=0.64[b]	rho=0.03; p=0.78[b]	rho=-0.05; p=0.65[b]
Disease duration from onset	z=1.02; p=0.31[a]	rho=-0.05; p=0.70[b]	rho=-0.06; p=0.62[b]	rho=-0.02; p=0.86[b]	rho=-0.13; p=0.28[b]	rho=-0.16; p=0.18[b]
Gender (male vs. female)	p=0.25[c]	z=-1.36; p=0.17[a]	z=1.37; p=0.17[a]	z=-1.55; p=0.12[a]	z=2.29; p=0.022[a]*	z=0.63; p=0.53[a]

[a]Rank sum test
[b]Spearman rank correlations
[c]Fishers exact test
*$P < 0.05$, **$P < 0.01$, ***$P < 0.005$
25/26 females were RT-QuIC positive whilst 41/48 males were RT-QuIC positive

Supplementary table 2. Associations between RT-QuIC parameters and clinical data for 74 Parkinson's disease patients. All data is estimate (95% confidence interval); p-value. Both exposures and outcomes standardised to unit standard deviation to aid interpretability. Adjusted for sex, age at lumbar puncture and disease duration from diagnosis at lumbar puncture, unless otherwise stated. Note that T_{lag} and T_{50} were inverted to normalise the distribution.

Clinical data	RT-QuIC positive response (odds ratios)	T_{lag}	V_{max}	T_{50}	F_{max}	AUC
MDS-UPDRS I	0.69 (0.35, 1.36); p=0.28	-0.20 (-0.44, 0.05); p=0.11	-0.17 (-0.41, 0.07); p=0.16	-0.33 (-0.56, -0.10); p=0.006*	-0.03 (-0.27, 0.21); p=0.82[a]	-0.15 (-0.40, 0.10); p=0.23
MDS-UPDRS II	0.80 (0.39, 1.66); p=0.55	-0.11 (-0.37, 0.14); p=0.38	-0.12 (-0.37, 0.13); p=0.34	-0.20 (-0.45, 0.06); p=0.13	-0.04 (-0.29, 0.22); p=0.78[a]	-0.04 (-0.30, 0.22); p=0.76
MDS-UPDRS III	0.92 (0.41, 2.05); p=0.84	-0.13 (-0.38, 0.11); p=0.29	-0.19 (-0.43, 0.05); p=0.12	-0.15 (-0.40, 0.09); p=0.22	-0.21 (-0.44, 0.03); p=0.090[a]	-0.19 (-0.43, 0.06); p=0.13
MDS-UPDRS IV	0.92 (0.39, 2.17); p=0.85	-0.03 (-0.27, 0.20); p=0.78	0.14 (-0.10, 0.38); p=0.24	-0.10 (-0.34, 0.13); p=0.38	0.09 (-0.14, 0.33); p=0.43[a]	0.01 (-0.23, 0.25); p=0.91
MMSE	1.88 (0.92, 3.84); p=0.084	0.20 (-0.04, 0.45); p=0.11	0.24 (-0.00, 0.49); p=0.052	0.26 (0.02, 0.51); p=0.037*	0.21 (-0.04, 0.45); p=0.094[a]	0.12 (-0.13, 0.38); p=0.34
MoCA	1.71 (0.76, 3.85); p=0.19	0.25 (-0.00, 0.50); p=0.053[a]	0.15 (-0.10, 0.41); p=0.24	0.33 (0.08, 0.58); p=0.010**	0.07 (-0.18, 0.33); p=0.58[a]	0.11 (-0.15, 0.37); p=0.39
Age at lumbar puncture	1.27 (0.60, 2.68); p=0.53	-0.01 (-0.25, 0.23); p=0.95	0.16 (-0.07, 0.40); p=0.17	0.07 (-0.17, 0.30); p=0.59	0.09 (-0.14, 0.33); p=0.42[a]	0.08 (-0.16, 0.32); p=0.53
Disease duration from diagnosis	0.78 (0.39, 1.57); p=0.49	0.04 (-0.21, 0.28); p=0.77	-0.01 (-0.25, 0.23); p=0.93	0.02 (-0.22, 0.27); p=0.84	-0.09 (-0.32, 0.15); p=0.47[a]	-0.09 (-0.33, 0.16); p=0.48
Gender (male vs. female)	0.25 (0.03, 2.27); p=0.22	-0.32 (-0.82, 0.18); p=0.21	-0.29 (-0.79, 0.20); p=0.24	-0.32 (-0.82, 0.18); p=0.21	-0.41 (-0.90, 0.08); p=0.10[a]	-0.03 (-0.53, 0.48); p=0.92

[a]Evidence the residuals are not normally distributed.
*P < 0.05, **P < 0.01, ***P < 0.005
UPDRS, Unified Parkinson's Disease Rating Scale; MDS-UPDRS, Movement Disorder Society Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental state examination

Supplementary table 3: Longitudinal follow-up associations in the UPDRS III (per SD change in transformed biomarker). Data is estimate (95% confidence interval); p-value. Adjusted associations are adjusted for age at diagnosis and sex. Note that T_{lag} and T_{50} were inverted to normalise the distribution.

MDS-UPDRS III	CRUDE ASSOCIATIONS		ADJUSTED ASSOCIATIONS	
	Intercept	**Slope (per year)**	**Intercept**	**Slope (per year)**
RT-QuIC positive response	0.52 (-10.11, 11.14); p=0.92[a]	-0.78 (-3.02, 1.46); p=0.50	0.44 (-10.06, 10.94); p=0.93[a]	-0.55 (-2.68, 1.58); p=0.61
T_{lag}	-0.35 (-3.48, 2.77); p=0.82[a]	-0.50 (-1.13, 0.14); p=0.13	-0.52 (-3.61, 2.58); p=0.74[a]	-0.32 (-0.94, 0.30); p=0.31
F_{max}	-1.57 (-4.77, 1.62); p=0.33[a]	-0.10 (-0.77, 0.56); p=0.76	-1.52 (-4.70, 1.67); p=0.35[a]	-0.08 (-0.71, 0.55); p=0.81
T_{50}	-0.05 (-3.17, 3.07); p=0.97[a]	-0.64 (-1.27, -0.01); p=0.046	-0.35 (-3.45, 2.75); p=0.82[a]	-0.48 (-1.09, 0.14); p=0.13[a]
V_{max}	-1.15 (-4.67, 2.38); p=0.52[a]	-0.19 (-0.97, 0.59); p=0.64	-1.32 (-4.82, 2.18); p=0.46[a]	-0.16 (-0.89, 0.58); p=0.68
AUC	-1.85 (-4.97, 1.27); p=0.25[a]	-0.18 (-0.85, 0.49); p=0.60	-1.97 (-5.04, 1.10); p=0.21[a]	-0.16 (-0.79, 0.47); p=0.62

[a]Evidence the random effects for that parameter are not normally distributed. Residuals showed little evidence they were not normally distributed.

Supplementary table 4: RT-QuIC parameters and ELISA biomarkers in the Discovery cohort against validated PD clinical clusters.
Data is mean ± SD (range) unless otherwise stated.

	Cluster 1 (n=27)	Cluster 2 (n=13)	Cluster 3 (n=15)	Cluster 4 (n=14)	*P* value
RT-QuIC positive response, n (%)	27 (100%)	9 (69.2%)	12 (80%)	13 (92.9%)	0.008
T_{lag}, hours	61.2 ± 21.8 (24.0-98.0)	73.5 ± 36.1 (30.0-120.0)	76.8 ± 28.0 (40.0-120.0)	62.6 ± 27.1 (30.0-120.0)	0.35
F_{max}, RFU x10^5	2.07 ± 0.71 (0.31-2.60)	1.62 ± 1.10 (0.20-2.60)	1.67 ± 0.99 (0.22-2.60)	1.81 ± 0.94 (0.21-2.60)	0.35[a]
T_{50}, hours	72.6 ± 23.1 (36.0-120.0)	81.8 ± 31.2 (48.0-120.0)	90.9 ± 24.7 (50.0-120.0)	75.6 ± 26.8 (37.0-120.0)	0.17[a]
V_{max} x10^4	5.41 ± 3.74 (0.25-16.43)	3.00 ± 3.53 (0.15-10.84)	2.91 ± 2.33 (0.20-7.90)	6.87 ± 7.18 (0.22-22.93)	0.018*
AUC x10^6	8.90 ± 4.99 (2.36-19.41)	9.74 ± 8.59 (2.04-21.59)	5.95 ± 3.42 (2.19-12.28)	8.00 ± 5.24 (0.14-19.85)	0.41
ELISA data					
αSyn (pg/mL)	763 ± 410 (285-1870)	534 ± 247 (289-1000)	557 ± 305 (147-1332)	511 ± 163 (280-900)	0.055
Aβ 1-42 (pg/mL)	579 ± 137 (335-889)	502 ± 123 (303-665)	550 ± 127 (302-754)	538 ± 105 (312-656)	0.42
p-tau (pg/mL)	44.9 ± 16.9 (10.3-72.3)	34.7 ± 14.6 (17.1-56.5)	40.9 ± 24.4 (10.3-103.6)	38.8 ± 12.9 (17.1-57.4)	0.45
p-tau/ Aβ 1-42	0.08 ± 0.03 (0.02-0.13)	0.07 ± 0.02 (0.04-0.10)	0.08 ± 0.05 (0.02-0.19)	0.08 ± 0.04 (0.03-0.15)	0.91

[a]K-Wallis test as the residuals showed evidence of non-normality. Five PD patients lacked the cluster data.

Supplementary table 5: Non-parametric associations between RT-QuIC parameters and clinical data for 23 multiple system atrophy patients. Spearman rank correlations, Rank sum test or a Fishers exact test. For the rank sum test a negative z indicates that higher scores of that continuous variable are more likely to have a positive response to the binary variable.

Clinical data	RT-QuIC positive	T_{lag}	V_{max}	T_{50}	F_{max}	AUC
MSA Subtype (MSA-C vs. MSA-P)	p=0.048[c]*	z=1.15; p=0.25[a]	z=-1.26; p=0.21[a]	z=1.22; p=0.22[a]	z=-1.65; p=0.098[a]	z=-1.83; p=0.068[a]
UMSARS Baseline	z=-0.14; p=0.89[a]	rho=0.27; p=0.2[b]	rho=-0.14; p=0.54[b]	rho=0.09; p=0.68[b]	rho=-0.02; p=0.93[b]	rho=-0.25; p=0.25[b]
UMSARS Follow-up[d]	z=-1.00; p=0.32[a]	rho=0.12; p=0.60[b]	rho=0.01; p=0.96[b]	rho=-0.05; p=0.85[b]	rho=0.14; p=0.57[b]	rho=-0.02; p=0.93[b]
UMSARS Change[e]	z=-2.93; p=0.003[a]**	rho=-0.54; p=0.013[b]*	rho=0.53; p=0.016[b]*	rho=-0.54; p=0.013[b]*	rho=0.54; p=0.015[b]*	rho=0.60; p=0.005[b]**
Age at lumbar puncture	z=0.11; p=0.92[a]	rho=0.16; p=0.45[b]	rho=-0.05; p=0.81[b]	rho=-0.07; p=0.76[b]	rho=-0.13; p=0.55[b]	rho=0.21; p=0.33[b]
Disease duration	z=-0.78; p=0.44[a]	rho=0.01; p=0.96[b]	rho=0.06; p=0.80[b]	rho=0.03; p=0.88[b]	rho=0.14; p=0.52[b]	rho=-0.11; p=0.63[b]
Gender (male vs. female)	p=[cf]	z=0.16; p=0.88[a]	z=-0.31; p=0.76[a]	z=0.09; p=0.92[a]	z=-0.25; p=0.80[a]	z=0.87; p=0.39[a]

[a]Rank sum test
[b]Spearman rank correlations
[c]Fishers exact test
[d]Only 20 patients had follow-up data
[e]Change from baseline to follow-up divided by number of years between assessments
[f] 7/10 females were RT-QuIC positive and 10/13 males were RT-QuIC positive
*P < 0.05, **P < 0.01, ***P < 0.005
MSA-C, Multiple System Atrophy-cerebellar type; MSA-P, Multiple System Atrophy-parkinsonian type; UMSARS, Unified Multiple System Atrophy Rating Scale.

Supplementary table 6. Longitudinal sample data from the DeNoPA cohort.

Case number (sex, year of birth)	Baseline visit CSF RT-QuIC result	Follow-up 1 CSF RT-QuIC result	Follow-up 2 CSF RT-QuIC result	DaT positivity	Conversion
Case 1 (M, *46)	positive	positive		↓	PD
Case 2 (F, *64)	negative	positive	positive	↓	PD
Case 3 (F, *53)	positive	positive		normal	
Case 4 (M, *47)	negative	negative		↓	DLB
Case 5 (M, *40)	negative			↓	
Case 6 (M, *49)	negative			↓	
Case 7 (M, *51)	negative			normal	
Case 8 (F, *40)	negative	positive		↓	
Case 9 (M, *40)	negative			↓	PD
Case 10 (F, *40)	negative			NA	
Case 11 (F, *51)	positive			normal	
Case 12 (M, *49)	negative	negative		↓	DLB
Case 13 (F, *63)	negative			normal	
Case 14 (M, *52)	positive	positive		↓	
Case 15 (M, *47)	negative			NA	DLB
Case 16 (M, *60)	negative			NA	
Case 17 (M, *62)	positive			NA	
Case 18 (F, *43)	negative			normal	PD

DLB, Dementia with Lewy bodies; NA, not available; PD, Parkinson's disease.

Supplementary table 7. Non-parametric associations between RT-QuIC parameters and clinical data for 45 idiopathic REM sleep behaviour disorder patients. All data is estimate (95% confidence interval); p-value. Clinical data and RT-QuIC parameters are all standardised to unit standard deviation to aid interpretability. Rank sum test, Spearman rank correlations or Fishers exact test. For the rank sum test a negative z indicates that higher scores of that continuous variable are more likely to have a positive response to the binary variable.

Clinical data	RT-QuIC positive response	T_{lag}	V_{max}	T_{50}	F_{max}	AUC
MDS-UPDRS I (n=24)	z=1.53; p=0.13[a]	rho=0.34; p=0.11[b]	rho=-0.33; p=0.12[b]	rho=0.34; p=0.10[b]	rho=-0.45; p=0.029[b]*	rho=-0.42; p=0.043[b]*
MDS-UPDRS II (n=24)	z=0.33; p=0.74[a]	rho=0.15; p=0.50[b]	rho=-0.12; p=0.58[b]	rho=0.17; p=0.43[b]	rho=-0.10; p=0.65[b]	rho=-0.11; p=0.61[b]
MDS-UPDRS III (n=35)	z=0.41; p=0.69[a]	rho=-0.02; p=0.93[b]	rho=-0.05; p=0.78[b]	rho=-0.01; p=0.97[b]	rho=-0.03; p=0.86[b]	rho=-0.07; p=0.69[b]
MMSE (n=45)	z=0.59; p=0.56[a]	rho=0.11; p=0.49[b]	rho=-0.10; p=0.52[b]	rho=0.11; p=0.48[b]	rho=-0.05; p=0.76[b]	rho=-0.04; p=0.78[b]
MoCA (n=34)	z=-0.88; p=0.38[a]	rho=-0.14; p=0.43[b]	rho=0.12; p=0.50[b]	rho=-0.13; p=0.45[b]	rho=0.14; p=0.43[b]	rho=0.09; p=0.60[b]
Age at lumbar puncture (n=45)	z=0.37; p=0.71[a]	rho=0.14; p=0.35[b]	rho=-0.09; p=0.54[b]	rho=0.16; p=0.29[b]	rho=-0.02; p=0.92[b]	rho=-0.05; p=0.75[b]
RBD duration (n=44)	z=1.38; p=0.17[a]	rho=0.20; p=0.19[b]	rho=-0.32; p=0.034[b]*	rho=0.25; p=0.10[b]	rho=-0.26; p=0.086[b]	rho=-0.21; p=0.17[b]
Gender (male vs. female) (n=45)	p=0.30[cd]	z=1.84; p=0.066[a]	z=-2.16; p=0.031[a]	z=1.71; p=0.088[a]	z=-2.54; p=0.011[a]	z=-2.52; p=0.012[a]
Urinary dysfunction (n=43)	p=0.53[c]	z=-1.30; p=0.20[a]	z=-0.62; p=0.53[a]	z=-1.14; p=0.25[a]	z=0.08; p=0.94[a]	z=-0.09; p=0.93[a]
Constipation (n=44)	p=0.75[c]	z=0.20; p=0.84[a]	z=-0.68; p=0.50[a]	z=0.31; p=0.75[a]	z=-0.81; p=0.42[a]	z=-0.81; p=0.42[a]
Family history (n=45)	p=0.39[c]	z=1.56; p=0.12[a]	z=-0.78; p=0.43[a]	z=1.87; p=0.061[a]	z=-1.62; p=0.10[a]	z=-0.97; p=0.33[a]
Hyposmia (n=34)	p=0.72[c]	z=0.08; p=0.94[a]	z=-0.51; p=0.61[a]	z=0.24; p=0.81[a]	z=-0.23; p=0.82[a]	z=-0.21; p=0.84[a]

[a]Rank sum test
[b]Spearman rank correlations
[c]Fishers exact test
[d] 6/12 females were RT-QuIC positive and 23/33 males were RT-QuIC positive
*$P < 0.05$, **$P < 0.01$, ***$P < 0.005$
UPDRS, Unified Parkinson's Disease Rating Scale; MDS-UPDRS, Movement Disorder Society Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental state examination

Supplementary table 8: Associations between RT-QuIC parameters and clinical data for the 45 RBD patients. All data is estimate (95% confidence interval); p-value. Both exposures and outcomes standardised to unit standard deviation to aid interpretability. Adjusted for sex, age at lumbar puncture and duration of disease. T_{lag} and T_{50} were inverted to normalise the distribution.

Clinical data	RT-QuIC positive response (odds ratios)	T_{lag}	V_{max}	T_{50}	F_{max}	AUC
MDS-UPDRS I (n=23)	0.45 (0.15, 1.29); p=0.14	-0.16 (-0.45, 0.12); p=0.24	-0.22 (-0.59, 0.15); p=0.23	-0.13 (-0.28, 0.02); p=0.087	-0.38 (-0.80, 0.03); p=0.066*	-0.34 (-0.67, 0.00); p=0.051*
MDS-UPDRS II (n=23)	1.31 (0.50, 3.44); p=0.58	0.02 (-0.28, 0.32); p=0.91	0.00 (-0.39, 0.40); p=0.99	-0.01 (-0.18, 0.16); p=0.93	-0.09 (-0.55, 0.37); p=0.70	-0.13 (-0.51, 0.25); p=0.48
MDS-UPDRS III (n=34)	0.72 (0.32, 1.60); p=0.42	-0.04 (-0.35, 0.26); p=0.78	-0.06 (-0.41, 0.28); p=0.70	-0.06 (-0.31, 0.19); p=0.60[a]	-0.16 (-0.56, 0.23); p=0.41	-0.23 (-0.64, 0.17); p=0.25
MMSE (n=44)	0.62 (0.28, 1.38); p=0.24	-0.25 (-0.55, 0.05); p=0.096	-0.32 (-0.60, -0.03); p=0.029*	-0.25 (-0.55, 0.05); p=0.11[a]	-0.18 (-0.47, 0.10); p=0.20	-0.23 (-0.52, 0.07); p=0.13
MoCA (n=33)	1.29 (0.57, 2.95); p=0.54	0.11 (-0.31, 0.52); p=0.60	-0.00 (-0.39, 0.39); p=0.99[a]	0.06 (-0.36, 0.49); p=0.76[a]	0.04 (-0.31, 0.39); p=0.81[a]	-0.02 (-0.34, 0.31); p=0.91
Age at lumbar puncture (n=44)	0.99 (0.50, 1.96); p=0.98	-0.14 (-0.45, 0.16); p=0.34	-0.15 (-0.44, 0.14); p=0.31	-0.15 (-0.45, 0.16); p=0.34[a]	-0.02 (-0.30, 0.27); p=0.90	-0.01 (-0.31, 0.29); p=0.95
RBD duration (n=44)	0.56 (0.28, 1.10); p=0.092	-0.20 (-0.51, 0.10); p=0.18	-0.27 (-0.56, 0.03); p=0.074	-0.21 (-0.52, 0.10); p=0.17[a]	-0.31 (-0.59, -0.02); p=0.034*	-0.21 (-0.51, 0.09); p=0.16
Gender (male vs. female) (n=44)	2.63 (0.64, 10.8); p=0.18	0.64 (-0.02, 1.30); p=0.059	0.79 (0.15, 1.43); p=0.017*	0.56 (-0.11, 1.23); p=0.097 [a]	0.90 (0.28, 1.52); p=0.005**	0.89 (0.24, 1.54); p=0.008**
Urinary dysfunction (n=42)	0.51 (0.12, 2.19); p=0.36	-0.66 (-1.30, -0.02); p=0.045*	-0.16 (-0.81, 0.48); p=0.61	-0.71 (-1.35, -0.07); p=0.032*	-0.17 (-0.79, 0.45); p=0.59	-0.08 (-0.74, 0.58); p=0.81
Constipation (n=43)	1.51 (0.40, 5.73); p=0.54	0.03 (-0.58, 0.65); p=0.92	0.10 (-0.48, 0.69); p=0.72	-0.02 (-0.64, 0.60); p=0.95[a]	0.25 (-0.31, 0.81); p=0.37	0.27 (-0.33, 0.86); p=0.37
Family history (n=44)	2.74 (0.26, 28.49); p=0.40	0.53 (-0.35, 1.41); p=0.23	0.15 (-0.72, 1.02); p=0.72[a]	0.67 (-0.22, 1.55); p=0.14[a]	0.47 (-0.36, 1.30); p=0.26	0.38 (-0.50, 1.25); p=0.39
Hyposmia (n=33)	1.84 (0.34, 9.88); p=0.47	0.07 (-0.78, 0.92); p=0.87	0.20 (-0.60, 0.99); p=0.62[a]	0.18 (-0.68, 1.05); p=0.67[a]	0.08 (-0.63, 0.80); p=0.81[a]	0.15 (-0.51, 0.81); p=0.65

[a]Evidence the residuals are not normally distributed.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.005$

UPDRS, Unified Parkinson's Disease Rating Scale; MDS-UPDRS, Movement Disorder Society Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental state examination