

Quantification of Lewy Body pathology by cerebrospinal fluid Endpoint Dilution RT-QuIC in a neuropathological autopsy cohort of clinically heterogeneous participants

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SUPPLEMENTARY METHODS

Assessment of Alzheimer's disease pathology

Alzheimer's disease neuropathologic changes (ADNC) were assessed in all LB-positive participants according to the National Institute on Aging-Alzheimer's Association (NIA-AA) criteria based on the Thal staging for A β plaques, Braak staging for neurofibrillary tangles and CERAD neuritic plaque score. The Thal's staging information was unavailable in a subset of participants (n=43, 25.6%). However, in 35 (81.4%), the final classification according to NIA-AA criteria could be unequivocally deduced from the Braak staging and the CERAD score. In a minority of participants (n=8), the final classification of ADNC changes could not be retrieved without the appropriate Thal staging (i.e., most could be categorized either as "Not AD, or "Low ADNC" or "Intermediate ADNC"). These were then excluded from the analyses in which precise ADNC staging was required.

Supplementary Table 1 – Neuropathological characteristics of whole LB-positive participants and stratified by neuropathological stage

	AD low, n (%)	AD intermediate, n (%)	AD high, n (%)	A β Thal staging, n ^a	Tau Braak Staging, n ^a	TDP-43 pathology, n (%)
LB-positive (n=168)	17/160, (10.6)	75/160 (46.9)	38/160 (23.7)	3.0 (1.0–4.0), 125	4.0 (3.2–5.0), 168	26/72 (36.1)
<ul style="list-style-type: none"> <i>Unified Staging System for Lewy Body Disorders</i> 						
<i>Olfactory bulb-only (n=8)</i>	0/7 (0.0)	3/7 (42.8)	2/7 (28.6)	3.0 (0.0–3.5), 5	4.0 (4.0–4.7), 8	2/5 (40.0)
<i>Brainstem predominant (n=30)</i>	2/29 (6.9)	15/29 (51.7)	3/29 (10.3)	2.0 (0.0–3.0), 25	4.0 (3.0–4.0), 30	3/10 (30.0)
<i>Limbic predominant (n=23)</i>	0/23 (0.0)	6/23 (26.1)	16/23 (69.6)	5.0 (3.5–5.0), 17	5.0 (5.0–6.0), 23	7/14 (50.0)
<i>Brainstem/Limbic (n=45)</i>	8/41 (19.5)	16/41 (39.0)	5/41 (12.2)	2.0 (0.0–3.0), 37	4.0 (3.0–4.0), 45	6/16 (37.5)
<i>Neocortical (n=62)</i>	7/60 (11.7)	35/60 (58.3)	12/60 (20.0)	3.0 (2.0–3.0), 41	4.0 (3.0–5.0), 62	8/27 (29.6)
<ul style="list-style-type: none"> <i>LP consensus criteria</i> 						
<i>Olfactory only (n=7)</i>	0/6 (0.0)	3/6 (50.0)	2/6 (33.3)	3.0 (0.7–3.7), 4	4.0 (4.0–5.0), 7	2/4 (50.0)
<i>Amygdala predominant (n=11)</i>	0/11 (0.0)	1/11 (9.1)	8/11 (72.7)	5.0 (2.2–5.0), 10	6.0 (5.0–6.0), 11	3/9 (33.3)
<i>Brainstem predominant (n=24)</i>	3/24 (12.5)	12/24 (50.0)	4/24 (16.7)	2.5 (0.7–4.0), 22	4.0 (4.0–4.7), 24	3/11 (27.3)
<i>Limbic (n=25)</i>	1/24 (4.2)	11/24 (45.8)	7/24 (29.2)	3.0 (0.5–4.0), 17	4.0 (3.5–5.0), 25	5/9 (55.5)
<i>Neocortical (n=101)</i>	13/95 (13.7)	48/95 (50.5)	17/95 (17.9)	3.0 (1.0–3.0), 72	4.0 (3.0–4.0), 101	13/39 (33.3)

a: expressed as median (interquartile range), number of participants with available data

Data on the staging of ADNC changes are available for 160 LB-positive participants. Data on the A β Thal staging are available for 125 LB-positive participants. Abbreviations: AD, Alzheimer’s disease; LB, Lewy Body

Supplementary Table 2 – Clinical and neuropathological characteristics of LB-positive/SAA-negative participants

	LB-density score	LB stage LPC	LB stage USSLB	ADNC staging	Clinical diagnosis	Age at death	Sex	MMSE	UPDRS part III	UPSIT
#1	1	Olfactory only	I	High	AD dementia	97	female	n/a	19	5
#2	2	Olfactory only	I	High	AD dementia	86	male	18	6	18
#3	3	Olfactory only	I	Intermediate	MCI	91	male	28	13	25
#4	1	Olfactory only	I	Intermediate	MCI	97	female	24	22	13
#5	1	Brainstem predominant	IIa	Intermediate	AD dementia	92	male	26	12	19
#6	1	Brainstem predominant	IIa	Not AD	Vascular PK	86	male	16	71	28
#7	3	Brainstem predominant	IIa	Intermediate	CU	90	male	27	15	11
#8	1	Brainstem predominant	IIa	High	AD dementia	80	male	5	50	23
#9	2	Brainstem predominant	IIa	Intermediate	MCI	101	female	20	5	35
#10	2	Brainstem predominant	IIa	Low	MCI	96	male	27	14	19
#11	1	Brainstem predominant	IIa	Intermediate	MCI	92	female	28	27	29
#12	2	Brainstem predominant	IIa	Not AD	FTD	98	female	9	1	34
#13	4	Amygdala predominant	IIb	High	AD dementia	90	female	9	17	13
#14	4	Amygdala predominant	IIb	High	AD dementia	83	male	5	15	12
#15	4	Amygdala predominant	IIb	Intermediate	PSP	82	male	25	4	33
#16	8	Amygdala predominant	IIb	High	AD dementia	85	female	18	2	31
#17	7	Amygdala predominant	IIb	High	AD dementia	78	female	5	n/a	15
#18	6	Limbic	III	Not AD	PSP	91	male	27	16	18
#19	6	Brainstem predominant	III	High	AD dementia	90	male	1	37	25

Abbreviations: AD, Alzheimer’s disease; ADNC, Alzheimer’s disease neuropathological changes; CU, clinically unimpaired; FTD, Frontotemporal dementia; LPC, Lewy Body Pathology consensus criteria; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; n/a, not available; PSP, progressive supranuclear palsy; UPDRS, Unified Parkinson’s Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test; USSLB, Unified Staging System for Lewy Body Disorders;

Supplementary Table 3– Clinical and neuropathological characteristics of LB-negative/SAA-positive participants

	log ₁₀ SD50	ADNC staging	Clinical diagnosis	Age at death	Sex	MMSE	UPDRS part III	UPSIT
#1	1.35	Intermediate	MCI	91	female	26	18	24
#2	2.31	Intermediate	AD dementia	96	female	18	9	13
#3	1.02	Not AD	Vascular dementia	95	male	26	34	24
#4	2.20	Intermediate	CU	87	female	30	0	27
#5	1.11	High	AD dementia	84	male	21	15	15
#6	1.36	Low	MSA	70	female	29	n/a	31

Abbreviations: AD, Alzheimer’s disease; ADNC, Alzheimer’s disease neuropathological changes; CU, clinically unimpaired; FTD, Frontotemporal dementia; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; n/a, not available; PSP, progressive supranuclear palsy; UPDRS, Unified Parkinson’s Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test

Supplementary Table 4 – LB-density scores and semiquantitative score values in the different sampled brain areas in the whole LB-positive/SAA-positive group and stratified by USSLB neuropathological stage

	LB-positive (n=149)	Olfactory bulb-only (n=4)	Brainstem predominant (n=22)	Limbic predominant (n=18)	Brainstem/limbic (n=43)	Neocortical (n=62)	p value
LB-density score	26.0 (14.0–32.5)	2.5 (1.2–3.7)	10.0 (6.7–15.7)	9.5 (6.7–13.0)	23.0 (21.0–27.0)	33.0 (30.0–35.0)	<0.0001
OBT	4.0 (3.0–4.0)	2.5 (1.2–3.0)	3.0 (2.0–4.0)	4.0 (3.7–4.0)	4.0 (3.0–4.0)	4.0 (4.0–4.0)	<0.0001
ME	4.0 (3.0–4.0)	0.0 (0.0–0.0)	3.0 (2.0–3.2)	0.5 (0.0–2.0)	4.0 (3.0–4.0)	4.0 (4.0–4.0)	<0.0001
LC	4.0 (3.0–4.0)	0.0 (0.0–0.0)	2.5 (1.0–3.0)	0.0 (0.0–1.0)	4.0 (3.0–4.0)	4.0 (4.0–4.0)	<0.0001
SN	3.0 (1.0–4.0)	0.0 (0.0–0.0)	1.0 (0.0–2.0)	0.0 (0.0–0.2)	3.0 (2.0–3.0)	3.5 (3.0–4.0)	<0.0001
AMG	4.0 (3.0–4.0)	0.0 (0.0–0.7)	1.0 (0.0–2.0)	3.5 (3.0–4.0)	4.0 (3.0–4.0)	4.0 (4.0–4.0)	<0.0001
TRANS	3.0 (1.0–4.0)	0.0 (0.0–0.0)	0.0 (0.0–1.0)	1.0 (0.0–2.0)	2.0 (2.0–3.0)	4.0 (3.0–4.0)	<0.0001
CI	2.0 (1.0–3.0)	0.0 (0.0–0.0)	0.0 (0.0–1.0)	0.0 (0.0–1.0)	2.0 (2.0–3.0)	4.0 (3.0–4.0)	<0.0001
TC	1.0 (0.0–2.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	1.0 (1.0–1.0)	3.0 (2.0–3.0)	<0.0001
FC	1.0 (0.0–2.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	1.0 (0.0–1.0)	2.0 (1.7–3.0)	<0.0001
PC	1.0 (0.0–2.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	1.0 (0.0–1.0)	2.0 (1.0–2.0)	<0.0001

P values of statistically significant comparisons are shown in bold.

Abbreviations: AMG, amygdala; CI, cingulate gyrus; FC, frontal cortex; LC, locus coeruleus; ME, medulla oblongata; SN, substantia nigra; OBT, olfactory bulb; PC, parietal cortex; TC, temporal cortex; TRANS, transentorhinal cortex

Supplementary Table 5 – Associations between SD50 values and semiquantitative scoring of LB pathology in the different sampled brain areas in the whole LB-positive/SAA-positive group and stratified by USSLB neuropathological stage

	LB-positive (n=149)		Olfactory bulb-only (n=4)		Brainstem predominant (n=22)		Limbic predominant (n=18)		Brainstem/limbic (n=43)		Neocortical (n=62)	
	Rho	p value	Rho	p value	Rho	p value	Rho	p value	Rho	p value	Rho	p value
OBT	0.18	0.03	0.95	0.17	0.21	0.34	-0.05	0.85	-0.03	0.82	-0.08	0.54
ME	0.57	<0.0001	-	-	0.66	0.0008	-0.04	0.87	0.09	0.58	0.06	0.65
LC	0.59	<0.0001	-	-	0.52	0.01	0.13	0.60	0.20	0.19	0.08	0.51
SN	0.57	<0.0001	-	-	0.34	0.11	0.15	0.54	0.29	0.07	0.09	0.50
AMG	0.37	<0.0001	-	-	0.59	0.004	-0.16	0.52	-0.13	0.40	0.14	0.28
TRANS	0.51	<0.0001	-	-	0.32	0.14	0.04	0.87	0.07	0.66	0.09	0.50
CI	0.59	<0.0001	-	-	0.46	0.03	0.38	0.11	0.23	0.13	-0.02	0.87
TC	0.60	<0.0001	-	-	0.19	0.38	0.21	0.40	0.29	0.06	0.10	0.42
FC	0.54	<0.0001	-	-	0.21	0.35	0.21	0.40	0.07	0.64	0.04	0.73
PC	0.57	<0.0001	-	-	0.19	0.38	-	-	0.23	0.14	0.07	0.58

P values of statistically significant associations are shown in bold.

Abbreviations: AMG, amygdala; CI, cingulate gyrus; FC, frontal cortex; LC, locus coeruleus; ME, medulla oblongata; SN, substantia nigra; OBT, olfactory bulb; PC, parietal cortex; TC, temporal cortex; TRANS, transentorhinal cortex

Supplementary Table 6 - Last available scores at clinical scales in the whole LB-positive/SAA-positive group and stratified by neuropathological stage

	MMSE ^a	UPDRS part III ^a	UPSIT ^a	Dementia, n (%)
Whole LB-positive/SAA-positive (n=149)	24.0 (17.0–27.0), 147	23.5 (7.0–42.0), 127	14.0 (10.0–19.0), 149	94 (63.1)
• <i>Unified Staging System for Lewy Body Disorders</i>				
<i>Olfactory bulb-only (Stage I) (n=4)</i>	28.5 (20.5–29.7), 4	13.0 (1.2–30.0), 4	22.5 (19.2–28.7), 4	1 (25.0)
<i>Brainstem predominant (Stage IIa) (n=22)</i>	27.0 (26.5–29.0), 21	6.5 (3.0–14.5), 20	21.0 (15.7–27.5), 22	5 (22.7)
<i>Limbic predominant (Stage IIb) (n=18)</i>	15.5 (6.7–24.0), 18	17.0 (4.0–50.1), 18	19.5 (12.0–26.7), 18	14 (77.8)
<i>Brainstem/Limbic (Stage III) (n=43)</i>	25.0 (20.7–27.0), 42	19.0 (7.0–40.0), 35	13.0 (10.0–19.0), 43	24 (55.8)
<i>Neocortical (Stage IV) (n=62)</i>	19.0 (13.7–26.0), 62	34.5 (23.5–52.6), 50	11.0 (10.0–14.0), 62	50 (80.6)
• <i>LP consensus criteria</i>				
<i>Olfactory only (n=3)</i>	28.0 (18.0–29.0), 3	21.0 (0.0–33.0), 3	20.0 (19.0–25.0), 3	1 (33.3)
<i>Amygdala predominant (n=6)</i>	15.5 (9.0–27.7), 6	16.5 (4.2–50.1), 6	30.0 (18.0–33.2), 6	4 (66.7)
<i>Brainstem predominant (n=15)</i>	27.0 (23.5–28.2), 14	6.0 (0.0–11.0), 15	23.0 (17.0–32.0), 15	4 (26.7)
<i>Limbic (n=24)</i>	24.0 (18.0–27.0), 24	14.0 (4.0–39.0), 23	15.0 (12.0–23.2), 24	13 (54.2)
<i>Neocortical (n=101)</i>	23.0 (15.2–27.0), 100	31.5 (14.2–45.0), 80	11.0 (10.0–15.5), 101	72 (71.3)

a: expressed as median (interquartile range), participants with available data.

Abbreviations: LB, Lewy Bodies; LP, Lewy Pathology; MMSE, Mini-Mental State Examination; SAA, seed amplification assay; UPDRS, Unified Parkinson's Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test.

Supplementary Table 7 - Clinical diagnoses in the whole LBD LB-positive/SAA-positive group and stratified by neuropathological stage

	Clinical diagnoses					
	PD	DLB	AD dementia	MCI	CU	Others
Whole LB-positive/SAA-positive (n=149)	69 (46.3)	13 (8.7)	29 (19.5)	8 (5.4)	19 (12.7)	11 (7.4)
• <i>Unified Staging System for Lewy Body Disorders</i>						
<i>Olfactory bulb-only (n=4)</i>	-	-	1 (25.0)	-	3 (75.0)	-
<i>Brainstem predominant (n=22)</i>	4 (18.2)	-	3 (13.6)	6 (27.3)	9 (49.5)	-
<i>Limbic predominant (n=18)</i>	1 (5.5)	-	10 (55.5)	1 (5.5)	2 (11.1)	4 (22.2) ^a
<i>Brainstem/Limbic (n=43)</i>	24 (55.8)	4 (9.3)	7 (16.3)	1 (2.3)	5 (11.6)	2 (4.6) ^b
<i>Neocortical (n=62)</i>	40 (64.5)	9 (14.5)	8 (12.9)	-	-	5 (8.1) ^c
• <i>LP consensus criteria</i>						
<i>Olfactory only (n=3)</i>	-	-	1 (33.3)	-	2 (66.7)	-
<i>Amygdala predominant (n=6)</i>	-	-	4 (66.7)	1 (16.7)	1 (16.7)	-
<i>Brainstem predominant (n=15)</i>	-	-	4 (26.7)	2 (13.3)	9 (60.0)	-
<i>Limbic (n=24)</i>	5 (20.8)	1 (4.2)	6 (25.0)	4 (16.7)	3 (12.5)	5 (20.8) ^d
<i>Neocortical (n=101)</i>	64 (63.4)	12 (11.9)	14 (13.9)	1 (1.0)	4 (4.0)	6 (5.9) ^e

a: include 2 participants with progressive supranuclear palsy, 1 participant with mixed dementia (vascular and degenerative) and 1 participant with not otherwise specified parkinsonism; b: include 2 participants with progressive supranuclear palsy; c: include 3 participants with mixed dementia (vascular and degenerative) and 2 participants with not otherwise specified parkinsonism; d: include 3 participants with progressive supranuclear palsy, 1 participant with mixed dementia (vascular and degenerative) and 1 participant with not otherwise specified parkinsonism; e: include 1 participant with progressive supranuclear palsy, 2 participants with not otherwise specified parkinsonism and 3 participants with mixed dementia (vascular and degenerative).

Abbreviations: AD, Alzheimer's Disease; CU, clinically unimpaired; DLB, Dementia with Lewy Bodies; MCI, mild cognitive impairment; LB, Lewy Bodies; LP, Lewy Pathology; MMSE, Mini-Mental State Examination; PD, Parkinson's Disease; SAA, seed amplification assay; UPDRS, Unified Parkinson's Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test.

Supplementary Table 8 - Last available scores at clinical scales in the LB-positive/SAA-positive pure LBD group and stratified by clinical diagnoses

	LB-positive/SAA-positive, pure LBD (n=43)	PD, pure LBD (n=30)	DLB, pure LBD (n=1)
MMSE ^a	27.0 (22.5–28.0), 42	25.5 (20.7–27.2), 30	-
UPDRS part III ^a	24.50 (7.0-44.2), 32	40.0 (27.0–47.0), 19	11, 1
UPSIT ^a	15.0 (10.0–19.0), 43	12.5 (10.0–16.2), 30	8, 1
Dementia, n (%)	22 (51.2)	19 (63.3)	1 (100)

a: expressed as median (interquartile range), participants with available data.

Abbreviations: LB, Lewy Bodies; LP, Lewy Pathology; MMSE, Mini-Mental State Examination; SAA, seed amplification assay; UPDRS, Unified Parkinson’s Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test.

Supplementary Table 9 - Clinical diagnoses in the LB-positive/SAA-positive pure LBD group and stratified by neuropathological stage

	Clinical diagnoses					
	PD	DLB	AD dementia	MCI	CU	Others
Whole LB-positive/SAA-positive, pure LBD (n=43)	30 (69.8)	1 (2.3)	1 (2.3)	4 (9.3)	6 (13.9)	1 (2.3)
• <i>Unified Staging System for Lewy Body Disorders</i>						
<i>Olfactory bulb-only (n=2)</i>	-	-	-	-	2 (100)	-
<i>Brainstem predominant (n=8)</i>	2 (25.0)	-	-	3 (37.5)	3 (37.5)	-
<i>Limbic predominant (n=1)</i>	-	-	-	1 (100)	-	-
<i>Brainstem/Limbic (n=19)</i>	16 (84.2)	1 (5.3)	-	-	1 (5.3)	1 (5.3) ^a
<i>Neocortical(n=13)</i>	12 (92.3)	-	1 (7.7)	-	-	-
• <i>LP consensus criteria</i>						
<i>Olfactory only (n=1)</i>	-	-	-	-	1 (100)	-
<i>Amygdala predominant (n=2)</i>	-	-	-	1 (50.0)	1 (50.0)	-
<i>Brainstem predominant (n=5)</i>	-	-	-	2 (40.0)	3 (60.0)	-
<i>Limbic (n=5)</i>	3 (60.0)	-	-	1 (20.0)	1 (20.0)	-
<i>Neocortical (n=30)</i>	27 (90.0)	1 (3.3)	1 (3.3)	-	-	1 (3.3) ^a

a: include 1 participant with progressive supranuclear palsy;

Abbreviations: AD, Alzheimer’s Disease; CU, clinically unimpaired; DLB, Dementia with Lewy Bodies; MCI, mild cognitive impairment; LB, Lewy Bodies; LP, Lewy Pathology; MMSE, Mini-Mental State Examination; PD, Parkinson’s Disease; SAA, seed amplification assay; UPDRS, Unified Parkinson’s Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test.

Supplementary Table 10 - Associations between LB-density scores and scores at clinical scales in the whole LB-positive/SAA-positive group and stratified by clinical diagnoses and AD co-pathology

	MMSE			UPDRS part III			UPSIT		
	n	Rho	p value	n	Rho	p value	n	Rho	p value
LB-positive/SAA positive									
<i>Whole (n=149)</i>	147	-0.23	0.004	127	0.47	<0.001	149	-0.50	<0.001
<i>Pure LBD (n=43)</i>	42	-0.29	0.06	32	0.70	<0.001	43	-0.60	<0.001
Parkinson's disease									
<i>Whole (n=69)</i>	69	-0.26	0.03	49	0.32	0.02	69	-0.14	0.22
<i>Pure LBD (n=30)</i>	30	-0.27	0.14	19	0.46	0.04	30	-0.41	0.02
Dementia with Lewy Bodies									
<i>Whole (n=13)</i>	12	-0.27	0.39	12	0.49	0.10	13	-0.53	0.06
<i>Pure LBD (n=1)</i>	0	-	-	1	-	-	1	-	-

Abbreviations: LB, Lewy Bodies; LBD, Lewy Body disease; MMSE, Mini-Mental State Examination; PD, Parkinson's disease; SAA, seed amplification assay; UPDRS, Unified Parkinson's Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test

Supplementary Table 11 - Associations between last available scores at clinical scales and LB-density score and semiquantitative scoring of LB pathology in the different sampled brain areas in the whole LB-positive/SAA-positive group

	MMSE (n=147)		UPDRS part III (n=127)		UPSIT (n=149)	
	Rho	p value	Rho	p value	Rho	p value
LB-density score	-0.23	0.004	0.47	<0.001	-0.50	<0.001
OBT	-0.24	0.003	0.17	0.05	-0.16	0.05
ME	-0.02	0.77	0.32	<0.001	-0.41	<0.001
LC	-0.03	0.68	0.36	<0.001	-0.46	<0.001
SN	-0.03	0.74	0.45	<0.001	-0.42	<0.001
AMG	-0.35	<0.001	0.38	<0.001	-0.35	<0.001
TRANS	-0.27	0.001	0.40	<0.001	-0.52	<0.001
CI	-0.21	0.01	0.41	<0.001	-0.48	<0.001
TC	-0.22	0.006	0.48	<0.001	-0.49	<0.001
FC	-0.22	0.007	0.42	<0.001	-0.43	<0.001
PC	-0.22	0.006	0.47	<0.001	-0.43	<0.001

P values of statistically significant associations are shown in bold.

Abbreviations: AMG, amygdala; CI, cingulate gyrus; FC, frontal cortex; LC, locus coeruleus; ME, medulla oblongata; MMSE, Mini-Mental State Examination; OBT, olfactory bulb; PC, parietal cortex; SN, substantia nigra; TC, temporal cortex; TRANS, transentorhinal cortex; UPDRS, Unified Parkinson's Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test.

Supplementary Table 12 - Time between available clinical scores and death in the whole LB-positive/SAA-positive group and stratified by clinical diagnoses

	MMSE	UPDRS part III	UPSIT
LB-positive/SAA positive			
<i>Whole (n=149)</i>	12.0 (7.0–22.2)	11.0 (6.0–21.0)	33.0 (19.5–50.5)
<i>Pure LBD (n=43)</i>	12.0 (7.0–23.0)	11.5 (5.2–23.7)	36.0 (23.0–48.0)
Parkinson's disease			
<i>Whole (n=69)</i>	11.0 (7.0–18.0)	11.0 (5.5–20.5)	31.0 (16.5–48.5)
<i>Pure LBD (n=30)</i>	10.5 (6.7–19.0)	10.0 (5.0–23.0)	35.0 (22.5–55.7)
Dementia with Lewy Bodies			
<i>Whole (n=13)</i>	12.5 (8.7–17.7)	9.5 (4.7–15.0)	34.0 (23.5–41.0)
<i>Pure LBD (n=1)</i>	-	2.0	1.0
AD dementia			
<i>Whole (n=29)</i>	12.0 (8.0–31.0)	10.5 (8.0–20.7)	49.0 (23.5–65.0)

Time is expressed in months and given as median (interquartile range)

Abbreviations: AD, Alzheimer's disease; LB, Lewy Bodies; LBD, Lewy Body disease; MMSE, Mini-Mental State Examination; SAA, seed amplification assay; UPDRS, Unified Parkinson's Disease Rating Scale; UPSIT, University of Pennsylvania Smell Identification Test.

Supplementary Table 13 – Performance of SD50 and clinical variables, alone or in combination, in the identification of participants at a LPC neocortical stage in the whole LB-positive/SAA-positive group and stratified by clinical diagnoses

	Cut-off	AUC (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
Whole LB-positive/SAA-positive group (n=149)				
log₁₀SD50 alone	>3.3	0.86 (0.79–0.92)	89.0 (82.0–94.0)	69.0 (55.0–80.0)
Dementia	-	0.63 (0.53–0.73)	71.0 (62.0–79.0)	54.0 (40.0–67.0)
UPSIT score	<19	0.80 (0.72–0.88)	88.0 (80.0–93.0)	58.0 (44.0–71.0)
log₁₀SD50>3.3 and dementia	-	0.78 (0.70–0.85)	63.0 (54.0–72.0)	92.0 (80.0–97.0)
log₁₀SD50>3.3 and UPSIT<19	-	0.79 (0.71–0.87)	77.0 (68.0–84.0)	81.0 (68.0–90.0)
Dementia and UPSIT<19	-	0.71 (0.62–0.80)	66.0 (57.0–75.0)	75.0 (61.0–85.0)
Alzheimer's disease dementia (n=29)				
log₁₀SD50 alone	>2.0	0.96 (0.89–1.0)	93.0 (69.0–100)	87.0 (62.0–98.0)
Dementia	-	-	-	-
UPSIT score	<15	0.83 (0.68–0.99)	93.0 (69.0–100)	67.0 (42.0–85.0)
log₁₀SD50>2.0 and dementia	-	0.90 (0.77–1.0)	93.0 (69.0–100)	87.0 (62.0–98.0)
log₁₀SD50>2.0 and UPSIT<15	-	0.90 (0.76–1.0)	86.0 (60.0–97.0)	93.0 (70.0–100)
Dementia and UPSIT<15	-	0.80 (0.63–0.97)	93.0 (69.0–100)	67.0 (42.0–85.0)

Only statistically significant comparisons are shown. Analyses in the Parkinson's disease participants are not shown due to the low number of subjects with a neuropathological stage different from neocortical.

Abbreviations AUC, area under the curve; CI, confidence interval; LB, Lewy Bodies; LPC, Lewy Pathology consensus criteria; SAA, seed amplification assay; UPSIT, University of Pennsylvania Smell Identification Test.