Table 1: Clinical demographic information of cases used in the study

Case	Sex	Age (yr)	BS: Tau	Thal phase	BS:LB	ARTAG	PMD (hr)
CN	Female	82	1	0	0	-	7.45
CN	Female	89	1	0	0	-	13
	2F	**85.5±1.75**					**10.2±1.3**
PSP	Male	77	2	0	3	+	5.4
PSP	Female	84	3	3	0	+	8.4
	1M/1F	**80.5±1.75**					**6.9±0.75**

Note: Average of demographic values are presented as mean ± standard error of mean (SEM, bold values); BS:Tau, Braak staging for Tau positivity; BS:LB, Braak staging for Lewy body; Thal phase amyloid staging where 0= no amyloid and 5= extensive amyloid spread; ARTAG, age related tau astrogliopathy; PMD, postmortem delay; yr, years; hr, hours.

Table 2: Histological analyses showing cell specific counting (density) of different astrocytic subtypes in different brain regions of CN and PSP cases (mean ±SEM)

Brain regions	CN (# cell/field)	PSP (# cell/field)	p-value
Frontal cortex			
Protoplasmic	109.28±5.924	129.95±6.104	0.34
Fibrous	19±1.571	17.49±0.572	0.88
IL-As	212.50±11.530	257.50±9.969	0.20
Vp-As	18.49±1.515	29.99±0.901	0.05
Tufted	6.245±0.596	18±2.150	0.02
AT8+ve	17±1.075	107.49±2.246	0.02
AT8+ve (subtype I)	8.50±0.649	29±3.206	0.02
AT8+ve (subtype II)	10.99±0.467	81±3.49	0.02
AT8-ve	66.99±4.990	3.99±.061	0.02
Temporal cortex			
Protoplasmic	68.81±5.644	24.98±1.952	0.02
Fibrous	62.49±5.248	29.75±1.744	0.02
IL-As	65.75±1.771	35.24±1.384	0.02
Vp-As	26±1.145	73.49±6.068	0.02
Thorn-shaped	17.49±7.603	18±2.215	0.68
Ramified	3.75±0.76	55.75±4.71	0.02
Granular/fuzzy	2.5±0.28	26±5.10	0.02
AT8+ve	4.24±0.72	75±3.80	0.02
AT8+ve (subtype I)		65.50±4.39	
AT8+ve (subtype II)	0.75±0.32	7.50±0.72	0.02
AT8-ve	43.25±7.29	43.25±7.29	0.05
As Plaque	8.25±7.029	63.49±7.28	0.02
Cerebellum			
Fibrous	71.18±1.39	10.12±19.270	0.02
Valate	100.42±3.13	183.12±16.93	0.02
Bergmann	144.43±4.26	201.13±3.98	0.02
Thorn-shaped	9.74±0.37	11.75±1.20	0.85
Ramified	17.24±0.54	27.76±0.94	0.02
Astrocytic plaque	36.32±1.28	50.50±1.18	0.02
AT8+ve	2.25±0.72	54.64±4.94	0.02
AT8+ve (subtype II)		34.55±4.094	
AT8-ve	80.63±6.25	5.49±1.19	0.02
Caudate nucleus			
Protoplasmic	58.77±2.46	45.48±2.22	0.11
Fibrous	22.50±2.25	43.71±3.13	0.11
Vp-As	0.49±0.022	3.99 ±0.68	0.14
Tufted	1.99±0.31	33.37±2.43	0.02
Thorn-shaped	6.76±0.60	1.38±0.60	0.34
Ramified	3.98±0.56	9.5±0.41	0.02
Granular/fuzzy	2.25±0.57	4.25±0.57	0.60
AT8+ve	3.25±0.54	41.24±3.02	0.02
AT8+ve (subtype I)	0.99±0.043	24±2.54	0.02
AT8+ve (subtype II)		16.49±1.86	

AT8-ve	29.75±2.73	3.5±1.24	0.02
Putamen			
Protoplasmic	16.51±1.28	24.24±3.34	0.51
Fibrous	18.25±2.09	18±2.57	0.88
Tufted	1.25±0.32	8.99±0.88	0.02
Thorn-shaped	7.75±0.72	14.74±1.84	0.34
Ramified	5.99±1.27	5.99±0.40	>0.9
Granular/fuzzy		9.25±0.60	
AT8+ve		66.75±10.6	
AT8+ve (subtype I)		36.75±7.78	
AT8+ve (subtype II)		27.24±3.38	
AT8-ve	83.25±4.77	1.25±0.54	0.02
As Plaque	0.75±0.21	12.5±2.99	0.02
Medulla Oblongata			
Protoplasmic	77.38±4.58	16±1.31	0.02
Fibrous	67.63±4.58	51.39±5.84	0.48
Tufted	3.75±0.65	17.75±1.87	0.02
Thorn-shaped	15±1.02	6.49±1.53	0.11
Ramified	2.74±0.21	7.23±0.48	0.02
Granular/fuzzy	1.24±0.42	13.49±1.10	0.02
AT8+ve	0.25±0.011	8.74±0.94	0.02
AT8+ve (subtype I)		2.99±0.75	
AT8+ve (subtype II)		3.75±0.89	
AT8-ve	52±2.05		
As Plaque		3.75±0.60	

Note: Counts of astrocytes were expressed as numbers per unit area and exact p-values are reported. IL-As, interlaminar astrocytes; Vp-As, varicose projection astrocytes; AT8+Ve, tau positive astrocytes; AT8+ve (subtype I), Tau infilterated astrocytic subtype I; AT8+ve (subtype II), Tau infilterated astrocytic subtype II; AT8-ve, tau negative astrocytes.

Supplementary Table 3: Detailed information regarding antibodies, chemicals and software used in the study

Reagent/ resources	Source	Identifier/ details
Antibodies		
rabbit anti-GFAP	Abcam	Cat # ab194324, RRID: AB_3662092
mouse anti-ICAM-1	Proteintech	Cat# CL594-60299, RRID:AB_2883457
mouse anti-S100B	EMD Milipore	Cat# MAB079-1, RRID:AB_571112
rabbit anti-GSK3B	Cell Signaling Technology	Cat # 9315S, RRID: AB_490890
mouse anti-AT8	Invitrogen	Cat# MN1020, RRID:AB_223647
rabbit anti-IBA-1	Invitrogen	Cat# PA5-27436, RRID:AB_2544912
NeuroTrace	ThermoFisher	Cat # N21479, RRID: AB_2341101
rabbit anti-Claudin 5	Abcam	Cat# ab131259, RRID:AB_11157940
DAPI	Milipore	
Goat anti-rabbit TRITC	Santa Cruz Biotechnology	Cat# sc-2780, RRID: AB_649006
Goat anti-mouse AlexaFluor 555	Thermo Fisher Scientific	Cat# A-21422, RRID: AB_2535844
Goat anti-mouse AlexaFluor 647	Abcam	Cat# ab150115, RRID: AB_2687948
Goat anti-mouse AlexaFluor 488	Thermo Fisher Scientific	Cat# A-11001, RRID: AB_2534069
Donkey anti-rabbit AlexaFluor 488	Thermo Fisher Scientific	Cat# A-21206, RRID: AB_2535792
Chemicals		
Mercury(II) chloride	Milipore	Cat # M1136, CAS: 7487-94-7
Potassium chromate	Milipore	Cat # 12249, CAS: 7789-00-6
Potassium di-chromate	Milipore	Cat # 207802, CAS: 7778-50-9
Ethyl alcohol	Milipore	Cat # 493511, CAS: 64-17-5
Sodium Thiosulfate	Milipore	Cat # 72049, CAS: 7772-98-7
Sodium chloride	Milipore	Cat # S9888, CAS: 7647-14-5
di-sodium hydrogen phosphate	Milipore	Cat # 1.06585, CAS: 7558-79-4
Triton X-100	Milipore	Cat # X100, CAS: 9036-19-5
Tween 20	Milipore	Cat # P1379, CAS: 9005-64-5
Software and algorithms		
Fiji 1.54p	*Schneider et al., (1)*	https://imagej.net/
Image J 1.53m	*Schneider et al., (1)*	https://imagej.net/
Imaris 10	Oxford Instrument	https://imaris.oxinst.com/
Inkscape 1.4.2	Inkscape project	https://inkscape.org/release/inkscape-1.4.2/windows/64-bit/msi/dl/
Wind rose plot	Jupiter notebook	https://pypi.org/project/windrose/1.6/
Simple Neurite Tracer	*Longhair et al.,(2)*	https://imagej.net/plugins/snt/
Neuron Studio	*Wearne et al., (3)*	https://biii.eu/neuronstudio

NeuroMorphoVis	*Abdellah et al., (4)*	https://github.com/BlueBrain/NeuroMorphoVis
Blender 3.1.0	Blender development team	https://www.blender.org/
Prism 10.1.1	GraphPad	https://www.graphpad.com/features

Note: Secondary antibodies were selected based on experimental design and spectral compatibility.

References:

1. J. Schindelin *et al.*, Fiji: an open-source platform for biological-image analysis. *Nat Methods* **9**, 676-682 (2012).
2. M. H. Longair, D. A. Baker, J. D. Armstrong, Simple Neurite Tracer: open source software for reconstruction, visualization and analysis of neuronal processes. *Bioinformatics* **27**, 2453-2454 (2011).
3. S. L. Wearne *et al.*, New techniques for imaging, digitization and analysis of three-dimensional neural morphology on multiple scales. *Neuroscience* **136**, 661-680 (2005).
4. M. Abdellah *et al.*, NeuroMorphoVis: a collaborative framework for analysis and visualization of neuronal morphology skeletons reconstructed from microscopy stacks. *Bioinformatics* **34**, i574-i582 (2018).