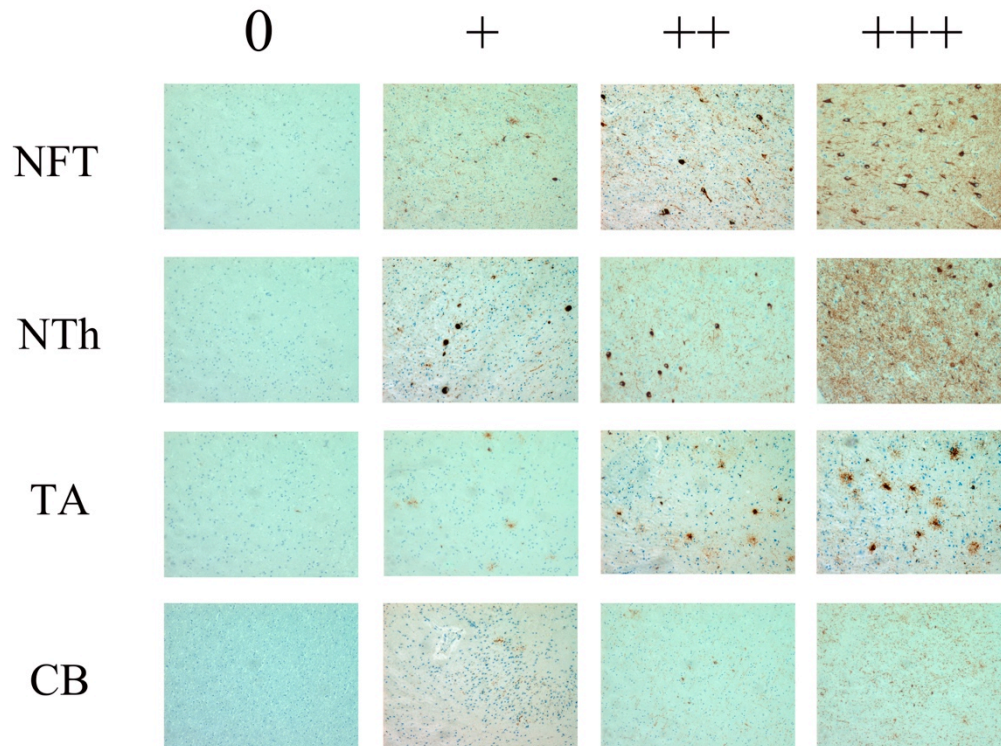


SUPPLEMENTARY MATERIAL

Supplementary figure 1.

Tau burden semi-quantitative analysis in the different cellular structures.

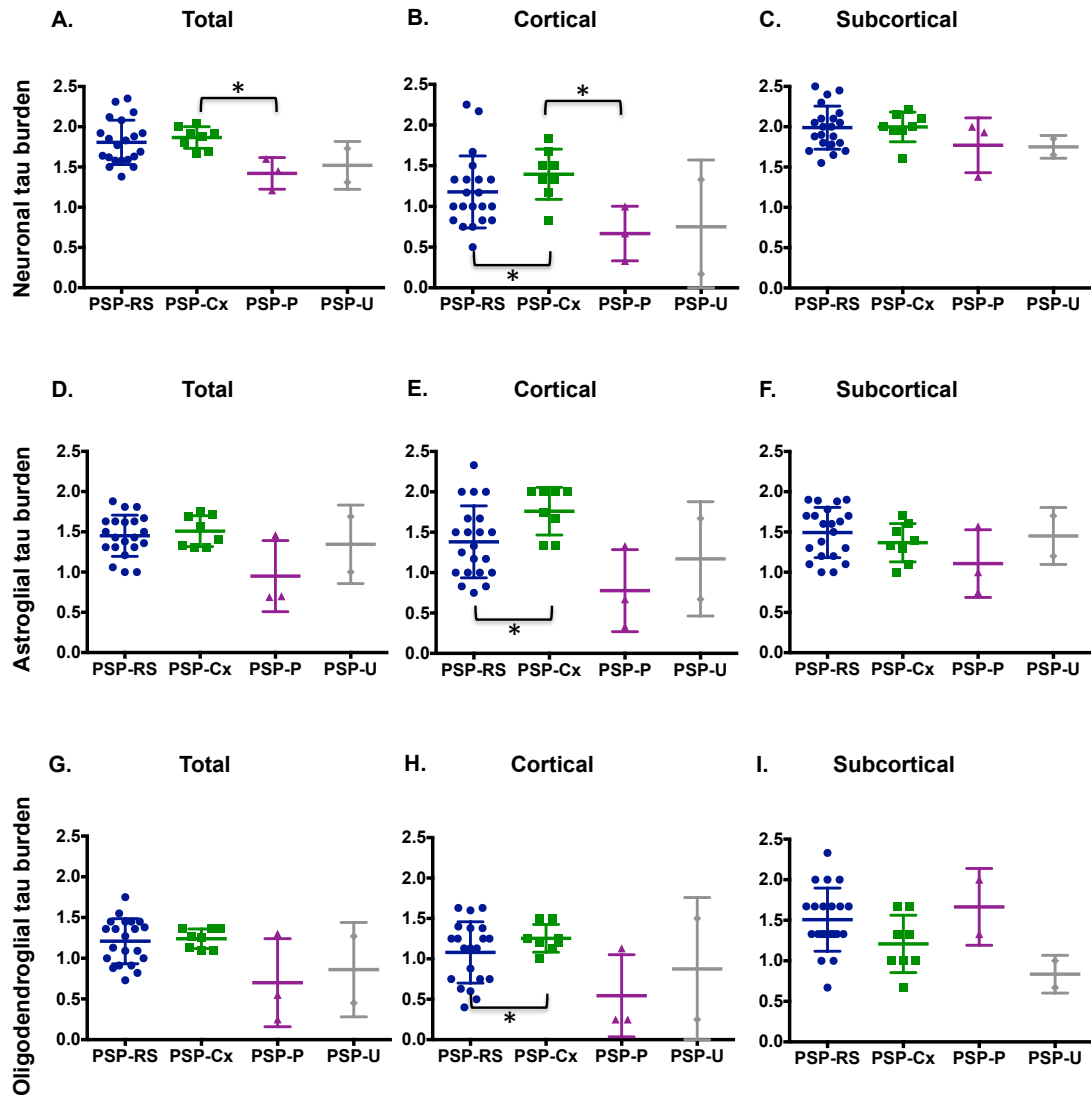
Images obtained at 10X magnification with immunohistochemistry for hyperphosphorylated tau



(AT8). Neurofibrillar tangles (NFT), Neuropyl threads (NTh), Tufted Astrocytes (TA) and Coiled bodies (CB) were measured. Intensity of deposits: 0 (absent), +(mild), ++ (moderate), +++(severe). Scale bar: 500 μ m.

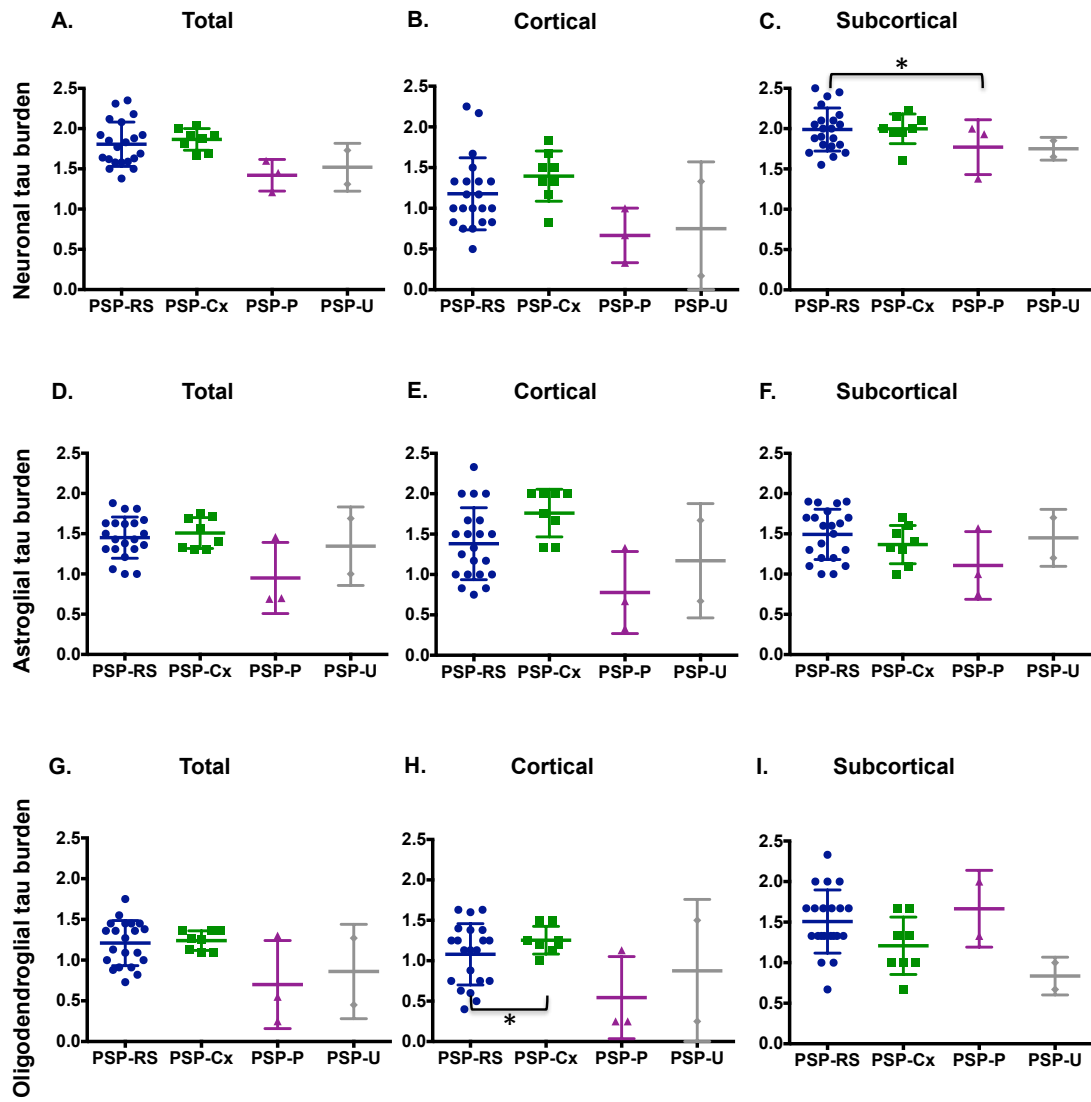
Supplementary figure 2.

RESPONDEK



Supplementary figure 3.

MDS-3Y



Supplementary Table 1. Respondek's criteria of predominant phenotypes of PSP.

Group	Feature	Impact
All subtypes	All of the following:	
	Adult onset	Mandatory
	Progression	
PSP-RS	All of the following within the first 2 years:	
	Postural instability	
	Falls	
	Abnormal saccades	Predominant
	Supranuclear gaze palsy	
PSP-PI	All of the following within the first 2 years:	
	Postural instability with falls	
	No supranuclear gaze palsy or abnormal saccades	Predominant
PSP-OM	All of the following within the first 2 years:	
	Supranuclear gaze palsy or abnormal saccades	Predominant
	No postural instability with falls	
PSP-P	At least two of the following:	
	Bradykinesia (any time)	
	Tremor (within the first 2 years)	Predominant
	Limb Rigidity (within the first 2 years)	
	Asymmetry at onset	
	Levodopa responsiveness	Supportive
PSP-P	Absence of all of the following within the first 2 years:	
	Falls	
	Postural instability	
	Supranuclear gaze palsy	Supportive
	Abnormal saccades	
	Frontal lobe dysfunction	
PSP-PAGF	All of the following within the first 2 years:	
	Bradykinesia	Predominant
	Freezing of gait or speech	
PSP-PAGF	Absence of all of the following within the first 2 years:	
	Tremor	
	Rigidity	Supportive
	Supranuclear gaze palsy and abnormal saccades	

	Falls and postural instability	
PSP-CBS	At least one extrapyramidal symptom:	
	Bradykinesia	
	Rigidity limbs > axial	
	Dystonia axial or extra-axial	
	At least one cortical symptom:	Predominant
	Apraxia of limb(s)	
	Myoclonus	
	Cortical sensory loss	
	Alien limb phenomenon	
	Asymmetry at onset	
	Persistent Asymmetry	Supportive
	No levodopa responsiveness	
PSP-FTD	Presence within the first 2 years of at least two of the following categories:	
	Frontal-type personality change	
	Social dysfunction	Predominant
	Executive dysfunction	
	Frontal behavior	
	Frontal physical signs	
	Presence of all of the following within the first 2 years:	
	Cognitive dysfunction	
	No AD-like deficits	Supportive
	No postural instability or falls	
	No supranuclear gaze palsy or abnormal saccades	
PSP-PNFA	At least one of the following:	
	Progressive non-fluent aphasia	Predominant
	Apraxia of speech	
	Absence of all of the following within the first 2 years:	
	Falls or postural instability	Supportive
	Supranuclear gaze palsy or abnormal saccades	
PSP-SD	Presence in the first 2 years:	Predominant
	Semantic dementia	
PSP-C	Presence in the first 2 years:	Predominant
	Cerebellar ataxia	

(Adapted from Respondek et al., 2014)

RS, Richardson's syndrome; PI, Postural Instability; OM, Oculomotor; P, Parkinsonism; PAGF, Pure Akinesia with Gait Freezing; CBS, Corticobasal Syndrome; FTD, Frontotemporal Dysfunction; PNFA, Progressive Non-Fluent Aphasia; SD, Semantic Dementia; C, Cerebellar.

Supplementary Table 2. Criteria application.

Case ID	Respondek	MDS-3y			MDS-6y			MDS-last		
		MDS criteria (O, P, A, C)	Predominance subtype and certain grade	MAX rules	MDS criteria (O, P, A, C)	Predominance subtype and certain grade	MAX rules	MDS criteria (O, P, A, C)	Predominance subtype and certain grade	MAX rules
34	PSP-C	O0, P2, A0, C0	unclassified	-	O0, P2, A0, C0	unclassified	-	O1, P2, A2, C3, CC2, CC3	prob. PSP-RS , poss. PSP-CBS, prob. PSP-P	MAX 1, 2
33	PSP-C	O2, O3, P1, A0, C0, CC2, CC3	prob. PSP-RS	-	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS	-	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 2
32	PSP-P	O0, P0, A3, C0	unclassified	-	O0, P0, A3, C0	unclassified	-	O3, P0, A2, A3, C0, CC2, CC3	s.o. PSP-P	-
31	PSP-P	O0, P0, A3, C0	unclassified	-	O1, P0, A2, A3, C0, CC2	prob. PSP-P	-	O1, P0, A2, A3, C0, CC2, CC3	prob. PSP-P	-
30	PSP-P	O0, P2, A3, C0	s.o. PSP-P	-	O0, P2, A3, C0	s.o. PSP-P	-	O0, P0, A2, A3, C0, CC2, CC3	s.o. PSP-P	-
29	PSP-P	O0, P0, A2, C0 CC1	s.o. PSP-P	-	O0, P0, A2, C0 CC1	s.o. PSP-P	-	O3, P0, A2, C0, CC2	s.o. PSP-P	-
28	PSP-FTD	O0, P0, A0, C2	unclassified	-	O0, P0, A0, C2	unclassified	-	O1, P0, A0, C2, CC2, CC3	prob. PSP-F	-
27	PSP-FTD	O0, P0, A0, C2	unclassified	-	O1, P0, A2, C2, CC2, CC3	prob. PSP-F , prob. PSP-P	MAX 2	O1, P0, A2, C2, CC2, CC3	prob. PSP-F , prob. PSP-P	MAX 2
26	PSP-FTD	O0, P0, A0, C2	unclassified	-	O1, P0, A2, C2, CC2, CC3	prob. PSP-F , prob. PSP-P	MAX 2	O1, P0, A2, C2, CC2, CC3	prob. PSP-F , prob. PSP-P	MAX 2
25	PSP-PPNFA	O0, P0, A0, C1	s.o. PSP-SL	-	O0, P0, A0, C1	s.o. PSP-SL	-	O0, P0, A2, C1, CC2, CC3	s.o. PSP-SL , s.o. PSP-P	MAX 2
24	PSP-PPNFA	O0, P0, A0, C1, CC2	s.o. PSP-SL	-	O1, P0, A2, C1, CC2	poss. PSP-SL, prob. PSP-P	MAX 1	O1, P0, A2, C1, CC2, CC3	poss. PSP-SL, prob. PSP-P	MAX 1
23	PSP-PPNFA	O0, P1, A2, C1, CC2	s.o. PSP-SL , s.o. PSP-P, s.o. PSP-PI	MAX 2	O1, P1, A2, C1, CC2, CC3	poss. PSP-SL, prob. PSP-RS , prob. PSP-P	MAX 1, 3	O1, P1, A2, C1, CC2, CC3	poss. PSP-SL, prob. PSP-RS , prob. PSP-P	MAX 1, 3
22	PSP-PPNFA	O1, P1, A0, C1	prob. PSP-RS , poss. PSP-SL	MAX 1	O1, P1, A2, C1, CC2, CC3	poss. PSP-SL, prob. PSP-RS , prob. PSP-P	MAX 1, 3	O1, P1, A2, C1, CC2, CC3	poss. PSP-SL, prob. PSP-RS , prob. PSP-P	MAX 1, 3
21	PSP-CBS	O1, P1, A0, C3	poss. PSP-CBS, prob. PSP-RS	MAX 1	O1, O3, P1, A2, C3, CC2, CC3	poss. PSP-CBS, prob. PSP-RS , prob. PSP-P	MAX 1, 3	O1, O3, P1, A2, C3, CC2, CC3	poss. PSP-CBS, prob. PSP-RS , prob. PSP-P	MAX 1, 3
20	PSP-CBS	O2, P1, A0, C3, CC2	prob. PSP-RS , poss. PSP-CBS	MAX 1	O2, P1, A2, C3, CC2	poss. PSP-CBS, prob. PSP-RS , prob. PSP-P	MAX 1, 3	O1, O3, P1, A2, C3, CC2, CC3	poss. PSP-CBS, prob. PSP-RS , prob. PSP-P	MAX 1, 3
19	PSP-PI	O0, P2, A2, C0	s.o. PSP-PI, s.o. PSP-P	MAX 3	O0, P2, A2, C0, CC2	s.o. PSP-PI, s.o. PSP-P	MAX 2	O0, P2, A2, C0, CC2	s.o. PSP-PI, s.o. PSP-P	MAX 2
18	PSP-PI	O0, P1, A2, C0, CC1	s.o. PSP-PI , s.o. PSP-P	MAX 3	O0, P1, A2, C2, CC1, CC3	s.o. PSP-PI , s.o. PSP-P, s.o. PSP-F	MAX 3	O0, P1, A2, C2, CC1, CC3	s.o. PSP-PI , s.o. PSP-P, s.o. PSP-F	MAX 3
17	PSP-PI	O0, P1, A0, C0	s.o. PSP-PI	-	O0, P1, A2, C0	s.o. PSP-PI , s.o. PSP-P	MAX 2	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3
16	PSP-PI	O0, P1, A2, C0	s.o. PSP-PI , s.o. PSP-P	MAX 3	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3
15	PSP-PI	O0, P1, A2, C0	s.o. PSP-PI , s.o. PSP-P	MAX 3	O1, P1, A2, C0, CC3	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3
14	PSP-PI	O0, P1, A0, C0	s.o. PSP-PI	-	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3
13	PSP-PI	O0, P1, A0, C0	s.o. PSP-PI	-	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3
12	PSP-PI	O1, P1, A0, C2	prob. PSP-RS , prob. PSP-F	MAX 2	O1, P1, A2, C2	prob. PSP-RS , prob. PSP-F, prob. PSP-P	MAX 2	O1, P1, A2, C2, CC2, CC3	prob. PSP-RS , prob. PSP-F, prob. PSP-P	MAX 2
11	PSP-PI	O1, P1, A0, C0	prob. PSP-RS	-	O1, P1, A0, C0, CC2, CC3	prob. PSP-RS	-	O1, P1, A0, C0, CC2, CC3	prob. PSP-RS	-
10	PSP-PI	O1, P1, A2, C0	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3
9	PSP-PI	O1, P1, A2, C0	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC3	prob. PSP-RS , prob. PSP-P	MAX 3
8	PSP-PI	O1, P1, A0, C0	prob. PSP-RS	-	O1, O3, P1, A2, C0, CC2	prob. PSP-RS , prob. PSP-P	MAX 2	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 2
7	PSP-RS	O1, P1, A3, C0	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, A3 C0	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, A3 C0	prob. PSP-RS , prob. PSP-P	MAX 3
6	PSP-RS	O1, P1, A0, C0	prob. PSP-RS	-	O1, P1, A2, C0	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0	prob. PSP-RS , prob. PSP-P	MAX 3
5	PSP-RS	O1, P1, A2, C0, CC2	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC2	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC2	prob. PSP-RS , prob. PSP-P	MAX 3
4	PSP-RS	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 3
3	PSP-RS	O1, P1, A0, C0, CC2, CC3	prob. PSP-RS	-	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 2	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 2
2	PSP-RS	O1, P1, A0, C0	prob. PSP-RS	-	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 2	O1, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 2
1	PSP-RS	O1, P1, A2, C0	prob. PSP-RS , prob. PSP-P	MAX 3	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 2	O1, O3, P1, A2, C0, CC2, CC3	prob. PSP-RS , prob. PSP-P	MAX 2

The table shows the operational values of the criteria used by Respondek et al. in 2014, the Movement Disorders Society (MDS) criteria and the MAX rules.

All patients met definite postmortem diagnosis of PSP and these criteria were applied retrospectively. Bold represents the phenotype selected after applicate the MAX rules when more than one phenotype was available.

MDS-3y, MDS criteria at 3 years of disease evolution; MDS-6y, MDS criteria at 6 years of disease evolution; MDS-last, MDS criteria at the last clinical assessment; RS, Richardson’s syndrome; PI, Postural Instability; OM, Oculomotor; P, Parkinsonism; CBS, Corticobasal Syndrome; FTD, Frontotemporal Dysfunction; PNFA, Progressive Non-Fluent Aphasia; SD, Semantic Dementia; C, Cerebellar; PSP-SL, PSP with predominant speech/language disorder; PSP-F, PSP with predominant frontal presentation; PSP-P, predominant parkinsonism; s.o., suggestive of; poss; possible; prob, probable.

Supplementary Table 3. Disease duration comparison between PSP phenotypes.

Phenotype classification	Cox's regression*	Hazard Ratio	95% IC		p-value
			Inferior	Superior	
Respondek	PSP-RS/PI vs. rest	2.503	1.069	5.863	0.035
	Rest vs. PSP-P	5.076	0.749	34.391	0.096
MDS-3y	PSP-RS/PI vs. rest	2.766	0.827	9.249	0.099
	Rest vs. PSP-P	11.03	0.724	167.981	0.084
MDS-6y	PSP-RS/PI vs. rest	3.105	1.078	8.945	0.036
	Rest vs. PSP-P	2.733	0.587	12.733	0.2
MDS-last	PSP-RS/PI vs. rest	4.581	1.612	13.023	0.004
	Rest vs. PSP-P	4.509	1.125	18.069	0.033

The table shows the Cox's regression for disease duration between PSP RS/PI vs. PSP-Cx + PSP-P (**PSP-RS/PI** vs. rest), and PSP-RS/PI + PSP-Cx vs. PSP-P (Rest vs **PSP-P**). * All of them were adjusted for age of onset and total tau burden. Respondek, criteria used by Respondek et al. in 2014; MDS-3y, MDS-PSP criteria at 3 years of disease evolution; MDS-6y, MDS-PSP criteria at 6 years; MDS-last; MDS-PSP criteria at the last clinical evaluation. PSP-RS/PI, Richardson Syndrome spectrum; PSP-Cx, PSP cortical predominant phenotypes; PSP-P, PSP with predominant parkinsonism.