Supplementary Information

Title: [^{18}F]Flortaucipir PET to autopsy comparisons in Alzheimer's and other neurodegenerative diseases

Supplementary Methods

MRI acquisition parameters

Amyloid-β PET acquisition and preprocessing details

Amyloid-β PET analyses

[^{18}F]Flortaucipir (FTP) PET acquisition and preprocessing details

FTP-PET W-score map details

FTP-PET region of interest (ROI) analysis details

Supplementary Tables

Supplementary Table 1: Distribution of neurofibrillary tangles on tau immunohistochemistry

Supplementary Tables 2-21: Distribution of non-neurofibrillary tangle tau pathology on tau immunohistochemistry

Supplementary Figures

Supplementary Figure 1: FTP-PET SUVR and W-score map images in patients with Alzheimer's disease autopsy diagnosis

Supplementary Figure 2: FTP-PET SUVR and W-score map images in patients with autopsy diagnoses of non-Alzheimer tauopathies, FTLD-TDP, and FTLD-FUS

Supplementary Figure 3: FTP-PET SUVR quantification at precentral gyrus, postcentral gyrus, and subcortical regions of interest with partial volume corrected data

Supplementary Figure 4: FTP-PET SUVR quantification of Braak stage regions of interest with partial volume corrected data

Supplementary References

Supplementary Methods

MRI acquisition parameters

Patients had the T1-weighted magnetization prepared rapid gradient echo (MPRAGE) sequence acquired either on a 3T Siemens Tim Trio or a 3T Siemens Prisma Fit scanner at University of California, San Francisco (UCSF). Both scanners had very similar acquisition parameters (sagittal slice orientation; slice thickness = 1.0 mm; slices per slab = 160; in-plane resolution = 1.0 x 1.0 mm; matrix = 240 x 256; repetition time = 2,300 ms; inversion time = 900 ms; flip angle = 9°), though echo time differed slightly (Trio= 2.98 ms; Prisma= 2.9ms).

The fourteen young, non-autopsy, cognitively normal controls had the T1-weighted MPRAGE sequence acquired on a 3T Siemens TIM Trio scanner at University of California, Berkeley (sagittal slice orientation; slice thickness = 1.0 mm; slices per slab = 160; in-plane resolution = 1.0 × 1.0 mm; matrix = 240x256; repetition time = 2300 ms; echo time = 2.98 ms; flip angle = 9°).

Amyloid-β PET acquisition and preprocessing details

Seventeen patients received an injection of ~15 mCi [^{11}C] Pittsburgh compound-B (PiB) and images were acquired on the Siemens Biograph PET/CT scanner at Lawrence Berkeley National Laboratory (LBNL). Thirteen patients underwent a full 90-minute acquisition, and four patients underwent a 50-70 minute post-injection acquisition. Distribution volume ratio (DVR) maps were created from 90-minute PET acquisitions. SUVR maps were created from 20-minute PET acquisitions; MRI and Freesurfer-defined cerebellar gray matter was used as the reference region (Villeneuve *et al.*, 2015).

One patient received an injection of ~10 mCi [^{18}F]Florbetapir and underwent a 50-70 minute post-injection acquisition on the GE Discovery STE/VCT PET/CT scanner at UCSF. Whole cerebellum was used as the reference region (Landau *et al*., 2013). Regardless of the type of

scan, attenuation correction and reconstruction were performed analogously to [^{18}F]Flortaucipir PET.

Amyloid-β PET analyses

The average DVR or SUVR was extracted from a large neocortical region of interest (ROI) encompassing frontal, cingulate, temporal, and parietal areas (Villeneuve *et al.*, 2015) and subsequently converted into Centiloid values using previously validated and published methods (Klunk *et al.*, 2015; La Joie *et al.*, 2019; Lesman-Segev *et al.*, 2019). A threshold of 24.4 Centiloids, which was previously shown to accurately identify intermediate-to-high ADNC, was used to determine amyloid-β PET positivity (La Joie *et al.*, 2019).

[^{18}F]Flortaucipir (FTP) PET acquisition and preprocessing details

For patients undergoing FTP-PET at LBNL, [^{18}F]FTP was synthesized and radiolabeled at the Lab's Biomedical Isotope Facility (Harrison *et al.*, 2019). For the patient scanned at UCSF, [^{18}F]FTP was provided by the Avid Radiopharmaceuticals clinical trials distribution network. LBNL scans have a resolution of 6.5 x 6.5 x 7.25 mm and UCSF scans have a resolution of 6.8 x 6.8 x 7.2 mm (based on Hoffman phantom).

FTP-PET W-score map details

Native-space FTP-PET SUVR images were warped to Montreal Neurological Institute (MNI) template-space using the deformation parameters derived from the MRI-based unified segmentation procedure using SPM12 (Ashburner and Friston, 2005). Warped SUVRs were masked to limit contamination from non-relevant areas (e.g. off-target binding from meninges, eyes, or skull) and smoothed with a 4 mm isotropic Gaussian kernel to be used for voxelwise analyses (La Joie *et al.*, 2018). Voxelwise FTP-PET W-score (i.e. covariate-adjusted Z-score) maps were computed from these SUVR images.

In the present study, we were interested in controlling for age as a covariate because older age is associated with increased off-target FTP binding in a regionally dependent manner (Choi

et al., 2018; Baker *et al.*, 2019). W-scores allow comparison of a patient's SUVR in a given voxel to the SUVR value expected for the patient's age, based on a normative dataset (La Joie *et al.*, 2018). Our normative sample consisted of 88 clinically and cognitively normal individuals from the Berkeley Aging Cohort between the age of 20 and 93 (mean age 66, standard deviation 20 years, 50% female) who underwent FTP-PET on the Biograph scanner. Cognitively normal individuals older than 60-years-old who were included in the normative dataset were amyloid-negative based on a PiB DVR < 10 Centiloids (Villeneuve *et al.*, 2015; Maass *et al.*, 2017).

FTP-PET region of interest (ROI) analysis details

Freesurfer cortical segmentation was used to define the precentral and postcentral gyrus (Desikan *et al.*, 2006), and subcortical segmentation was used to define globus pallidus and putamen ROIs (Fischl *et al.*, 2002). An MNI-space version of the Talairach atlas (Wake Forest University Pickatlas Toolbox) was used to define the subthalamic nucleus and substantia nigra ROIs (Maldjian *et al.*, 2003). Lastly, an MNI-space cerebellar atlas (SUIT template) was used to define the dentate nucleus ROI (Diedrichsen *et al.*, 2009, 2011). All ROIs in MNI-space were reverse-normalized to native space for each subject prior to extraction of SUVR values.

Supplementary Tables

Supplementary Table 1: Distribution of neurofibrillary tangles on tau immunohistochemistry

	Case ID	*A1*	*A2*	*A3*	*A4*	*A5*	*A6*	*A7*	*A8*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*
Braak NFT Stage	**Anatomical Region**	**AD, LBD (VI)**	**AD, LBD (VI)**	**AD, LBD (VI)**	**AD (VI)**	**AD (VI)**	**AD (VI)**	**AD (VI)**	**AD (VI)**	**PSP (II)**	**PSP (II)**	**PSP (II)**	**PSP, AD (III)**	**CBD (I)**	**CBD, HS, TDP-43 unclassifiable (III)**	**FTLD-tau (*MAPT* P301L), AD (IV)**	**FTLD-tau (*MAPT* S301I), HS (0)**	**AGD (III)**	**TDP-43 type A (*GRN*) (I)**	**TDP-43 type B (*C9orf72*) (I)**	**FTLD-FUS (0)**
I	Entorhinal cortex	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	
II	CA1/subiculum	X	X	X	X	X	X	X	X	X	X	X	X		X	X		X			
	CA2	X	X	X	X	X	X		X						X						
	CA3-4	X	X	X	X	X	X	X	X				X		X	X					
III	Amygdala	X	X	X		X	X	X	X				X		X	X		X			
IV	Anterior cingulate	X	X	X	X	X	X	X	X				X								
	Inferior temporal gyrus	X	X	X	X	X	X	X	X				X			X		X			
	Middle temporal gyrus	X						X													
V	Superior temporal gyrus	X						X													
	Inferior frontal gyrus	X	X				X														
	Middle frontal gyrus	X	X	X	X	X	X	X	X				X								
	Superior frontal sulcus		X				X														
	Angular gyrus	X	X	X	X	X	X	X	X												
VI	Precentral gyrus	X	X	X	X	X	X	X	X												

	Postcentral gyrus	X	X	X	X	X	X	X	X											
	Calcarine/striate cortex	X	X	X		X	X		X											
	Lateral occipital cortex						X		X											
Region	**Anatomical Subregion**																			
Other cortex	Dentate gyrus	X	X	X	X		X	X	X											
	Middle insula																			
	Frontal pole																			
	Anterior orbital gyrus																			
Subcortical	Ventral striatum																			
	Putamen																			
	Globus pallidus																			
	Subthalamic nucleus																			
	Thalamus																			
Cerebellum	Cerebellar dentate nucleus		X																	
	Cerebellar folia																			
Midbrain	Substantia nigra	X	X	X	X	X		X	X									X		
	Tectum	X		X		X			X											
	Periaqueductal gray	X		X	X				X											
	Dorsal raphe	X		X	X	X	X	X	X							X				
	Oculomotor nucleus	X																X		

	Trochlear nucleus	X	X																		
Pons	Locus ceruleus	X	X	X	X	X	X	X	X												
	Median raphe	X	X		X	X	X	X	X									X			
	Abducens nucleus	X																			
	Facial nucleus	X																			
Medulla	Hypoglossal nucleus																				
	Dorsal afferent nucleus, vagus																				
	Nucleus solitary tract																				
	Olive																				

AD = Alzheimer's Disease; AGD = Argyrophilic Grain Disease; CBD = Corticobasal Degeneration; HS = Hippocampal Sclerosis; NFT = Neurofibrillary Tangle; LBD = Lewy Body Disease; PSP = Progressive Supranuclear Palsy; FTLD = Frontotemporal Lobar Degeneration; TDP-43 = TAR DNA-Binding Protein 43; FUS = Fused in Sarcoma

The neuroanatomical structures used for determination of Braak neurofibrillary tangle staging are noted in the first two columns in the top half of the table. Other evaluated neuroanatomical structures are noted in the bottom half of the table. The columns to the right of the double lines show the distribution of neurofibrillary tangle pathology for each patient. Each patient's primary and contributing autopsy diagnoses and Braak staging of neurofibrillary tangle pathology are noted at the top of each column. The orange highlighting indicates locations that were evaluated with tau (CP-13 antibody) immunohistochemistry. Each "X" indicates a location where neurofibrillary tangles were documented by the pathologist.

Supplementary Tables 2-21: Distribution of non-neurofibrillary tangle tau pathology on tau immunohistochemistry

Table ID	***Supplementary Table 2***
Case ID	***A1***
Primary, Contributing Pathology (Braak NFT Stage)	**Alzheimer's Disease, Lewy Body Disease (VI)**
Incidental Tau Pathology	**Argyrophilic Grain Disease**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular & Perinuclear Ring Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**None**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex							X	X
II	CA1/subiculum							X	
	CA2					X		X	
	CA3-4							X	
III	Amygdala							X	
IV	Anterior cingulate							X	X
	Inferior temporal gyrus							X	X
	Middle temporal gyrus							X	X
V	Superior temporal gyrus							X	X
	Inferior frontal gyrus							X	X
	Middle frontal gyrus							X	X
	Superior frontal sulcus								
	Angular gyrus							X	X
VI	Precentral gyrus							X	X
	Postcentral gyrus							X	X
	Calcarine/striate cortex							X	X
	Lateral occipital cortex								
Region	**Anatomical Subregion**								

Other cortex	Dentate gyrus							**X**	**X**
	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra							**X**	
	Tectum							**X**	
	Periaqueductal gray							**X**	
	Dorsal raphe							**X**	
	Oculomotor nucleus							**X**	
	Trochlear nucleus							**X**	
Pons	Locus ceruleus							**X**	
	Median raphe							**X**	
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

GCI = Glial Cytoplasmic Inclusions; NCI = Neuronal Cytoplasmic Inclusions; NFT = Neurofibrillary Tangle

Each patient's primary and contributing autopsy diagnoses and Braak staging of neurofibrillary tangle pathology are noted at the top of each table. Incidental non-Alzheimer tau pathology and the types of neuronal and glial cytoplasmic inclusions present are noted below the primary and

contributing autopsy pathology. The orange highlighting indicates locations that were evaluated with tau (CP-13 antibody) immunohistochemistry. Each "X" indicates a location were non-neurofibrillary tangle tau pathology was documented by the pathologist.

Table ID	*Supplementary Table 3*
Case ID	*A2*
Primary, Contributing Pathology (Braak NFT Stage)	**Alzheimer's Disease, Lewy Body Disease (VI)**
Incidental Tau Pathology	**Argyrophilic Grain Disease**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular & Perinuclear Ring Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**None**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex							**X**	**X**
II	CA1/subiculum							**X**	
	CA2					**X**		**X**	
	CA3-4							**X**	
III	Amygdala							**X**	
IV	Anterior cingulate							**X**	**X**
	Inferior temporal gyrus							**X**	**X**
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus							**X**	**X**
	Middle frontal gyrus							**X**	**X**
	Superior frontal sulcus							**X**	**X**
	Angular gyrus							**X**	**X**
VI	Precentral gyrus							**X**	**X**
	Postcentral gyrus							**X**	**X**
	Calcarine/striate cortex							**X**	**X**
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus							**X**	**X**

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus							**X**	
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra							**X**	
	Tectum							**X**	
	Periaqueductal gray							**X**	
	Dorsal raphe								
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe							**X**	
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 4*
Case ID	*A3*
Primary, Contributing Pathology (Braak NFT Stage)	**Alzheimer's Disease, Lewy Body Disease (VI)**
Incidental Tau Pathology	**Aging-Related Tau Astrogliopathy**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Astrocytic Inclusions**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex							**X**	**X**
II	CA1/subiculum							**X**	
	CA2					**X**		**X**	
	CA3-4							**X**	
III	Amygdala						**X**	**X**	**X**
IV	Anterior cingulate							**X**	**X**
	Inferior temporal gyrus							**X**	**X**
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus							**X**	**X**
	Superior frontal sulcus								
	Angular gyrus							**X**	**X**
VI	Precentral gyrus							**X**	**X**
	Postcentral gyrus							**X**	**X**
	Calcarine/striate cortex							**X**	**X**
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus							**X**	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra							**X**	
	Tectum							**X**	
	Periaqueductal gray							**X**	
	Dorsal raphe							**X**	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe							**X**	
	Abducens nucleus							**X**	
	Facial nucleus							**X**	
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 5*
Case ID	*A4*
Primary, Contributing Pathology (Braak NFT Stage)	**Alzheimer's Disease (VI)**
Incidental Tau Pathology	**Argyrophilic Grain Disease**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Argyrophilic Thorny Astrocytes in Clusters (1), Coiled Bodies (2)**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					**X**	**2**	**X**	**X**
II	CA1/subiculum					**X**	**2**	**X**	
	CA2					**X**		**X**	
	CA3-4					**X**		**X**	
III	Amygdala						**2**	**X**	**X**
IV	Anterior cingulate							**X**	**X**
	Inferior temporal gyrus							**X**	**X**
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus						**1, 2**	**X**	**X**
	Superior frontal sulcus								
	Angular gyrus						**1**	**X**	
VI	Precentral gyrus							**X**	
	Postcentral gyrus							**X**	
	Calcarine/striate cortex								
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus							**X**	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus						**1, 2**	**X**	**X**
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra							**X**	
	Tectum							**X**	
	Periaqueductal gray							**X**	
	Dorsal raphe							**X**	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe							**X**	
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 6*
Case ID	*A5*
Primary, Contributing Pathology (Braak NFT Stage)	**Alzheimer's Disease (VI)**
Incidental Tau Pathology	**Argyrophilic Grain Disease**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					X	X	X	
II	CA1/subiculum					X	X	X	X
	CA2					X		X	
	CA3-4					X		X	
III	Amygdala					X		X	
IV	Anterior cingulate					X		X	X
	Inferior temporal gyrus					X	X	X	X
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus					X	X	X	X
	Superior frontal sulcus								
	Angular gyrus					X	X	X	X
VI	Precentral gyrus					X	X	X	X
	Postcentral gyrus					X	X	X	X
	Calcarine/striate cortex					X	X	X	X
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					X		X	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra					**X**		**X**	
	Tectum					**X**		**X**	
	Periaqueductal gray					**X**		**X**	
	Dorsal raphe					**X**		**X**	
	Oculomotor nucleus					**X**		**X**	
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe					**X**		**X**	
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 7*
Case ID	*A6*
Primary, Contributing Pathology (Braak NFT Stage)	**Alzheimer's Disease (VI)**
Incidental Tau Pathology	**None**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**None**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex							**X**	**X**
II	CA1/subiculum					**X**		**X**	
	CA2					**X**		**X**	
	CA3-4							**X**	
III	Amygdala							**X**	**X**
IV	Anterior cingulate							**X**	**X**
	Inferior temporal gyrus							**X**	**X**
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus							**X**	**X**
	Middle frontal gyrus							**X**	**X**
	Superior frontal sulcus							**X**	**X**
	Angular gyrus							**X**	**X**
VI	Precentral gyrus							**X**	**X**
	Postcentral gyrus							**X**	**X**
	Calcarine/striate cortex							**X**	**X**
	Lateral occipital cortex							**X**	**X**
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus							**X**	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra								
	Tectum								
	Periaqueductal gray								
	Dorsal raphe							**X**	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe							**X**	
	Abducens nucleus							**X**	
	Facial nucleus							**X**	
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 8*
Case ID	*A7*
Primary, Contributing Pathology (Braak NFT Stage)	**Alzheimer's Disease (VI)**
Incidental Tau Pathology	**Argyrophilic Grain Disease**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					X	X	X	X
II	CA1/subiculum					X	X	X	
	CA2					X		X	
	CA3-4					X		X	
III	Amygdala					X	X		
IV	Anterior cingulate							X	X
	Inferior temporal gyrus					X		X	X
	Middle temporal gyrus							X	
V	Superior temporal gyrus							X	
	Inferior frontal gyrus								
	Middle frontal gyrus							X	X
	Superior frontal sulcus								
	Angular gyrus							X	
VI	Precentral gyrus							X	
	Postcentral gyrus							X	
	Calcarine/striate cortex							X	
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					X		X	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra					**X**		**X**	
	Tectum							**X**	
	Periaqueductal gray					**X**		**X**	
	Dorsal raphe							**X**	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe							**X**	
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 9*
Case ID	*A8*
Primary, Contributing Pathology (Braak NFT Stage)	**Alzheimer's Disease (VI)**
Incidental Tau Pathology	**Argyrophilic Thorny Astrocytes in Clusters, Argyrophilic Grain Disease**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Argyrophilic Thorny Astrocytes in Clusters (1), Coiled Bodies (2)**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					**X**	**2**	**X**	**X**
II	CA1/subiculum					**X**	**2**	**X**	
	CA2					**X**		**X**	
	CA3-4					**X**		**X**	
III	Amygdala					**X**		**X**	**X**
IV	Anterior cingulate							**X**	**X**
	Inferior temporal gyrus							**X**	**X**
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus						**1**	**X**	**X**
	Superior frontal sulcus								
	Angular gyrus						**1**	**X**	**X**
VI	Precentral gyrus						**1**	**X**	**X**
	Postcentral gyrus							**X**	
	Calcarine/striate cortex							**X**	
	Lateral occipital cortex							**X**	**X**
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					**X**		**X**	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra					**X**		**X**	
	Tectum							**X**	
	Periaqueductal gray							**X**	
	Dorsal raphe					**X**		**X**	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus					**X**		**X**	
	Median raphe							**X**	
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 10*
Case ID	*1*
Primary, Contributing Pathology (Braak NFT Stage)	**Progressive Supranuclear Palsy (II)**
Incidental Tau Pathology	**None**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex			X		X	X	X	
II	CA1/subiculum			X		X	X	X	
	CA2								
	CA3-4					X		X	
III	Amygdala			X		X	X	X	
IV	Anterior cingulate	X		X		X	X		X
	Inferior temporal gyrus								
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus	X		X	X	X	X	X	X
	Middle frontal gyrus	X		X	X	X	X		X
	Superior frontal sulcus	X		X	X	X	X	X	X
	Angular gyrus			X		X	X	X	X
VI	Precentral gyrus			X		X		X	
	Postcentral gyrus							X	
	Calcarine/striate cortex							X	
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					X		X	X

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus			X		X	X	X	
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus	X				X	X	X	
	Cerebellar folia						X		
Midbrain	Substantia nigra	X				X		X	
	Tectum	X				X		X	
	Periaqueductal gray	X				X		X	
	Dorsal raphe								
	Oculomotor nucleus	X				X		X	
	Trochlear nucleus								
Pons	Locus ceruleus								
	Median raphe								
	Abducens nucleus	X				X		X	
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 11*
Case ID	*2*
Primary, Contributing Pathology (Braak NFT Stage)	**Progressive Supranuclear Palsy (II)**
Incidental Tau Pathology	**Aging-Related Tau Astrogliopathy**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular or Tangle-like Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies (1), Subependymal Thorn-Shaped Astrocytes (2)**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					**X**	**1**	**X**	**X**
II	CA1/subiculum					**X**		**X**	
	CA2							**X**	
	CA3-4							**X**	
III	Amygdala			**X**		**X**	**1, 2**	**X**	
IV	Anterior cingulate			**X**		**X**	**1**	**X**	**X**
	Inferior temporal gyrus			**X**		**X**	**1**	**X**	**X**
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus			**X**	**X**	**X**	**1**	**X**	**X**
	Middle frontal gyrus			**X**	**X**	**X**	**1**	**X**	**X**
	Superior frontal sulcus								
	Angular gyrus			**X**		**X**	**1**	**X**	**X**
VI	Precentral gyrus			**X**	**X**	**X**	**1**	**X**	**X**
	Postcentral gyrus			**X**	**X**	**X**	**1**	**X**	**X**
	Calcarine/striate cortex								
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus							**X**	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus			**X**		**X**		**X**	**X**
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus	**X**				**X**	**1**	**X**	**X**
	Cerebellar folia						**1**	**X**	**X**
Midbrain	Substantia nigra	**X**				**X**	**1**	**X**	
	Tectum	**X**				**X**	**1**	**X**	**X**
	Periaqueductal gray	**X**				**X**	**1**	**X**	
	Dorsal raphe	**X**				**X**	**1**	**X**	
	Oculomotor nucleus	**X**				**X**	**1**	**X**	**X**
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe	**X**				**X**		**X**	
	Abducens nucleus	**X**				**X**	**1**	**X**	**X**
	Facial nucleus	**X**					**1**		
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 12*
Case ID	*3*
Primary, Contributing Pathology (Braak NFT Stage)	**Progressive Supranuclear Palsy (II)**
Incidental Tau Pathology	**Argyrophilic Grain Disease, Aging-Related Tau Astrogliopathy**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular, Fibrillary, or Ring-like Perinuclear Inclusions (R)**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies (1), Aging-Related Tau Astrogliopathy (2)**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex			**X**		**X**	**1**	**X**	**X**
II	CA1/subiculum					**X**		**X**	
	CA2					**R**			
	CA3-4			**X**					
III	Amygdala			**X**		**X**	**1, 2**	**X**	
IV	Anterior cingulate								
	Inferior temporal gyrus			**X**		**X**	**1**		**X**
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus			**X**		**X**	**1**		**X**
	Middle frontal gyrus			**X**		**X**	**1**		**X**
	Superior frontal sulcus			**X**		**X**	**1**		**X**
	Angular gyrus			**X**		**X**	**1**		**X**
VI	Precentral gyrus			**X**		**X**	**1**	**X**	**X**
	Postcentral gyrus			**X**		**X**	**1**		**X**
	Calcarine/striate cortex			**X**		**X**			
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus			**X**		**X**			

	Middle insula								
	Frontal pole			**X**		**X**	**1**		**X**
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus	**X**		**X**		**X**	**1**		
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra					**X**		**X**	
	Tectum								
	Periaqueductal gray								
	Dorsal raphe								
	Oculomotor nucleus					**X**		**X**	
	Trochlear nucleus								
Pons	Locus ceruleus								
	Median raphe								
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 13*
Case ID	*4*
Primary, Contributing Pathology (Braak NFT Stage)	**Progressive Supranuclear Palsy, Alzheimer's Disease (III)**
Incidental Tau Pathology	**Argyrophilic Grain Disease, Aging-Related Tau Astrogliopathy**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex			X		X	X	X	X
II	CA1/subiculum					X		X	X
	CA2					X		X	
	CA3-4					X		X	
III	Amygdala			X		X		X	X
IV	Anterior cingulate	X		X	X		X	X	X
	Inferior temporal gyrus			X		X		X	X
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus	X		X	X		X	X	X
	Superior frontal sulcus	X		X	X		X	X	X
	Angular gyrus								
VI	Precentral gyrus	X		X	X		X	X	X
	Postcentral gyrus			X			X		
	Calcarine/striate cortex			X				X	
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					X		X	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus	**X**		**X**	**X**		**X**	**X**	**X**
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus	**X**				**X**	**X**	**X**	**X**
	Cerebellar folia								
Midbrain	Substantia nigra	**X**		**X**		**X**		**X**	
	Tectum	**X**		**X**		**X**		**X**	
	Periaqueductal gray	**X**		**X**		**X**		**X**	
	Dorsal raphe								
	Oculomotor nucleus	**X**						**X**	
	Trochlear nucleus								
Pons	Locus ceruleus								
	Median raphe								
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 14*
Case ID	*5*
Primary, Contributing Pathology (Braak NFT Stage)	**Corticobasal Degeneration (I)**
Incidental Tau Pathology	**None**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex		**X**			**X**	**X**	**X**	**X**
II	CA1/subiculum					**X**		**X**	
	CA2					**X**		**X**	
	CA3-4					**X**		**X**	
III	Amygdala		**X**			**X**	**X**	**X**	
IV	Anterior cingulate		**X**			**X**	**X**	**X**	**X**
	Inferior temporal gyrus		**X**			**X**	**X**	**X**	**X**
	Middle temporal gyrus		**X**			**X**	**X**	**X**	**X**
V	Superior temporal gyrus		**X**			**X**	**X**	**X**	**X**
	Inferior frontal gyrus		**X**			**X**	**X**	**X**	**X**
	Middle frontal gyrus		**X**			**X**	**X**	**X**	**X**
	Superior frontal sulcus		**X**			**X**	**X**	**X**	**X**
	Angular gyrus		**X**			**X**	**X**	**X**	**X**
VI	Precentral gyrus		**X**			**X**	**X**	**X**	**X**
	Postcentral gyrus		**X**			**X**	**X**	**X**	**X**
	Calcarine/striate cortex								
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					**X**			**X**

	Middle insula		X			X	X	X	X
	Frontal pole		X			X	X	X	X
	Anterior orbital gyrus		X			X	X		X
Subcortical	Ventral striatum					X		X	
	Putamen					X	X	X	X
	Globus pallidus					X	X	X	
	Subthalamic nucleus					X	X	X	
	Thalamus		X			X	X	X	X
Cerebellum	Cerebellar dentate nucleus					X	X	X	X
	Cerebellar folia					X			X
Midbrain	Substantia nigra					X	X	X	
	Tectum					X	X	X	
	Periaqueductal gray					X	X	X	
	Dorsal raphe					X	X	X	
	Oculomotor nucleus					X		X	
	Trochlear nucleus					X		X	
Pons	Locus ceruleus					X		X	
	Median raphe					X		X	
	Abducens nucleus					X		X	X
	Facial nucleus					X		X	X
Medulla	Hypoglossal nucleus							X	
	Dorsal afferent nucleus, vagus					X		X	
	Nucleus solitary tract					X		X	
	Olive					X	X	X	X

Table ID	*Supplementary Table 15*
Case ID	*6*
Primary, Contributing Pathology (Braak NFT Stage)	**Corticobasal Degeneration, Hippocampal Sclerosis (Left), TDP-43 Unclassifiable (III)**
Incidental Tau Pathology	**Argyrophilic Grain Disease**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular or Compact/round Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies (Common) & Spider-Like Astrocytic Inclusions (Rare)**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex		X			X	X	X	X
II	CA1/subiculum					X	X	X	
	CA2					X	X	X	
	CA3-4					X	X	X	
III	Amygdala		X			X	X	X	
IV	Anterior cingulate		X			X	X	X	X
	Inferior temporal gyrus		X			X	X	X	X
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus		X			X	X	X	X
	Superior frontal sulcus								
	Angular gyrus		X			X	X	X	X
VI	Precentral gyrus		X			X	X	X	X
	Postcentral gyrus					X	X	X	X
	Calcarine/striate cortex					X	X	X	X
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					X	X	X	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra					**X**	**X**	**X**	
	Tectum					**X**	**X**	**X**	**X**
	Periaqueductal gray					**X**	**X**	**X**	
	Dorsal raphe					**X**	**X**	**X**	
	Oculomotor nucleus					**X**	**X**	**X**	
	Trochlear nucleus								
Pons	Locus ceruleus					**X**		**X**	
	Median raphe					**X**		**X**	
	Abducens nucleus					**X**	**X**	**X**	**X**
	Facial nucleus					**X**	**X**	**X**	**X**
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 16*
Case ID	*7*
Primary, Contributing Pathology (Braak NFT Stage)	**FTLD-tau (*MAPT* P301L), Alzheimer's Disease (IV)**
Incidental Tau Pathology	**None**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions & Compact/round Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Astrocytic, Resembling Bushy Astrocytes**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					X	X	X	X
II	CA1/subiculum					X	X	X	
	CA2					X	X	X	
	CA3-4					X		X	
III	Amygdala					X	X	X	X
IV	Anterior cingulate					X	X	X	X
	Inferior temporal gyrus					X	X	X	X
	Middle temporal gyrus					X	X	X	X
V	Superior temporal gyrus					X	X	X	X
	Inferior frontal gyrus					X	X	X	X
	Middle frontal gyrus					X	X	X	X
	Superior frontal sulcus					X	X	X	X
	Angular gyrus						X	X	
VI	Precentral gyrus					X	X	X	
	Postcentral gyrus						X	X	
	Calcarine/striate cortex					X	X	X	
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					X	X		

	Middle insula					X	X	X	X
	Frontal pole					X	X	X	X
	Anterior orbital gyrus					X	X	X	X
Subcortical	Ventral striatum					X	X	X	X
	Putamen					X	X	X	
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus					X	X	X	
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra					X		X	
	Tectum					X		X	
	Periaqueductal gray					X		X	
	Dorsal raphe					X		X	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus					X		X	
	Median raphe					X		X	
	Abducens nucleus					X		X	
	Facial nucleus					X		X	
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 17*
Case ID	*8*
Primary, Contributing Pathology (Braak NFT Stage)	**FTLD-tau (*MAPT* S301I), Hippocampal Sclerosis (Right) (0)**
Incidental Tau Pathology	**None**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions (Common) & Round/ovoid Inclusions (Occasional)**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies, Ramified Astrocytes, "Spider-like" Inclusions**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					X	X	X	X
II	CA1/subiculum					X		X	
	CA2					X		X	
	CA3-4					X		X	
III	Amygdala					X	X	X	X
IV	Anterior cingulate					X	X	X	X
	Inferior temporal gyrus					X	X	X	X
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus					X	X	X	X
	Middle frontal gyrus					X	X	X	X
	Superior frontal sulcus								
	Angular gyrus					X	X	X	X
VI	Precentral gyrus					X	X	X	X
	Postcentral gyrus					X	X	X	X
	Calcarine/striate cortex					X	X	X	X
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					X		X	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum					X		X	X
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus					X		X	X
	Cerebellar folia					X	X	X	X
Midbrain	Substantia nigra					X		X	
	Tectum					X	X	X	
	Periaqueductal gray					X		X	
	Dorsal raphe					X		X	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus					X		X	
	Median raphe					X		X	
	Abducens nucleus					X	X	X	X
	Facial nucleus					X	X	X	X
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 18*
Case ID	*9*
Primary, Contributing Pathology (Braak NFT Stage)	**Argyrophilic Grain Disease (III)**
Incidental Tau Pathology	**None**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions (i.e. Pre-tangles)**
Glial Cytoplasmic Inclusion (GCI) Type	**Coiled Bodies**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					**X**	**X**	**X**	
II	CA1/subiculum					**X**	**X**	**X**	
	CA2					**X**	**X**	**X**	
	CA3-4								
III	Amygdala					**X**	**X**	**X**	
IV	Anterior cingulate					**X**		**X**	
	Inferior temporal gyrus					**X**			
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus								
	Superior frontal sulcus								
	Angular gyrus								
VI	Precentral gyrus							**X**	
	Postcentral gyrus								
	Calcarine/striate cortex								
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus					**X**	**X**		

	Middle insula								
	Frontal pole							**X**	
	Anterior orbital gyrus					**X**			
Subcortical	Ventral striatum							**X**	
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra							**X**	
	Tectum								
	Periaqueductal gray								
	Dorsal raphe								
	Oculomotor nucleus							**X**	
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe							**X**	
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 19*
Case ID	*10*
Primary, Contributing Pathology (Braak NFT Stage)	**TDP-43 type A (*GRN*) (I)**
Incidental Tau Pathology	**None**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**None**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					**X**		**X**	**X**
II	CA1/subiculum							**X**	
	CA2								
	CA3-4								
III	Amygdala					**X**		**X**	
IV	Anterior cingulate								
	Inferior temporal gyrus								
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus								
	Superior frontal sulcus								
	Angular gyrus								
VI	Precentral gyrus								
	Postcentral gyrus								
	Calcarine/striate cortex								
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus							**X**	

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra								
	Tectum								
	Periaqueductal gray								
	Dorsal raphe								
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus								
	Median raphe								
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 20*
Case ID	*11*
Primary, Contributing Pathology (Braak NFT Stage)	**TDP-43 type B (*C9orf72*) (I)**
Incidental Tau Pathology	**Atypical Tauopathy with Glial and Perivascular Tau Deposits**
Neuronal Cytoplasmic Inclusion (NCI) Type	**Diffuse/granular Inclusions**
Glial Cytoplasmic Inclusion (GCI) Type	**Astrocytic Inclusions (Involving Proximal Process of Astroglia)**

Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex					**X**		**X**	
II	CA1/subiculum								
	CA2								
	CA3-4								
III	Amygdala					**X**	**X**	**X**	
IV	Anterior cingulate								
	Inferior temporal gyrus					**X**	**X**	**X**	
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus					**X**		**X**	
	Superior frontal sulcus								
	Angular gyrus								
VI	Precentral gyrus								
	Postcentral gyrus								
	Calcarine/striate cortex								
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus								

	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra								
	Tectum								
	Periaqueductal gray								
	Dorsal raphe					**X**		**X**	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe							**X**	
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Table ID	*Supplementary Table 21*
Case ID	*12*
Primary, Contributing Pathology (Braak NFT Stage)	**FTLD-FUS (0)**
Incidental Tau Pathology	**None**
Neuronal Cytoplasmic Inclusion (NCI) Type	**None**
Glial Cytoplasmic Inclusion (GCI) Type	**None**

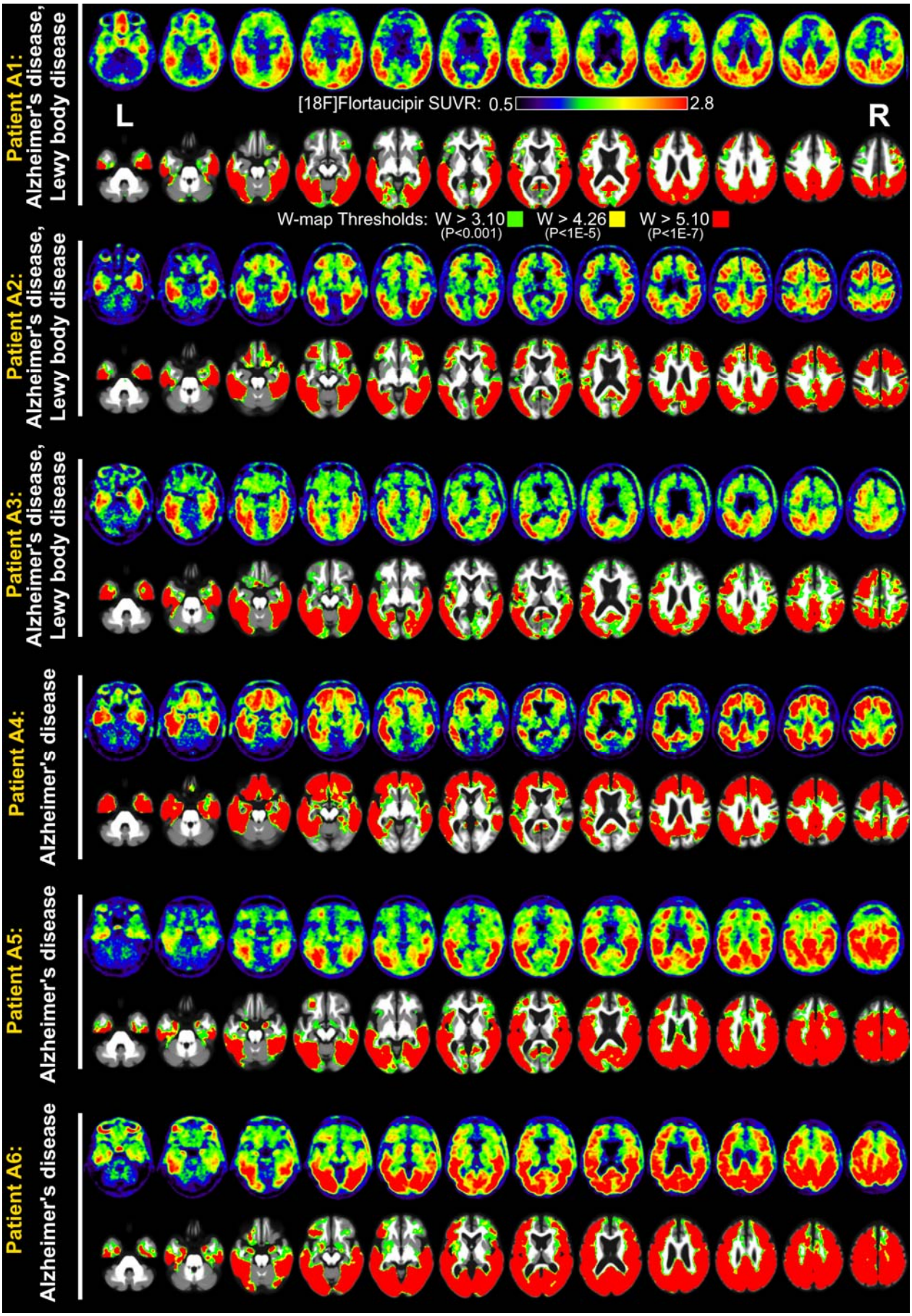
Braak NFT Stage	**Anatomical Region**	**Globose Tangles**	**Astrocytic Plaques**	**Tufted Astrocytes**	**Thorny Astrocytes**	**NCI**	**GCI**	**Grey Matter (Neuropil) Threads/ Grains**	**White Matter Threads/ Grains**
I	Entorhinal cortex							X	
II	CA1/subiculum								
	CA2								
	CA3-4								
III	Amygdala								
IV	Anterior cingulate								
	Inferior temporal gyrus								
	Middle temporal gyrus								
V	Superior temporal gyrus								
	Inferior frontal gyrus								
	Middle frontal gyrus								
	Superior frontal sulcus								
	Angular gyrus								
VI	Precentral gyrus								
	Postcentral gyrus								
	Calcarine/striate cortex								
	Lateral occipital cortex								
Region	**Anatomical Subregion**								
Other cortex	Dentate gyrus								

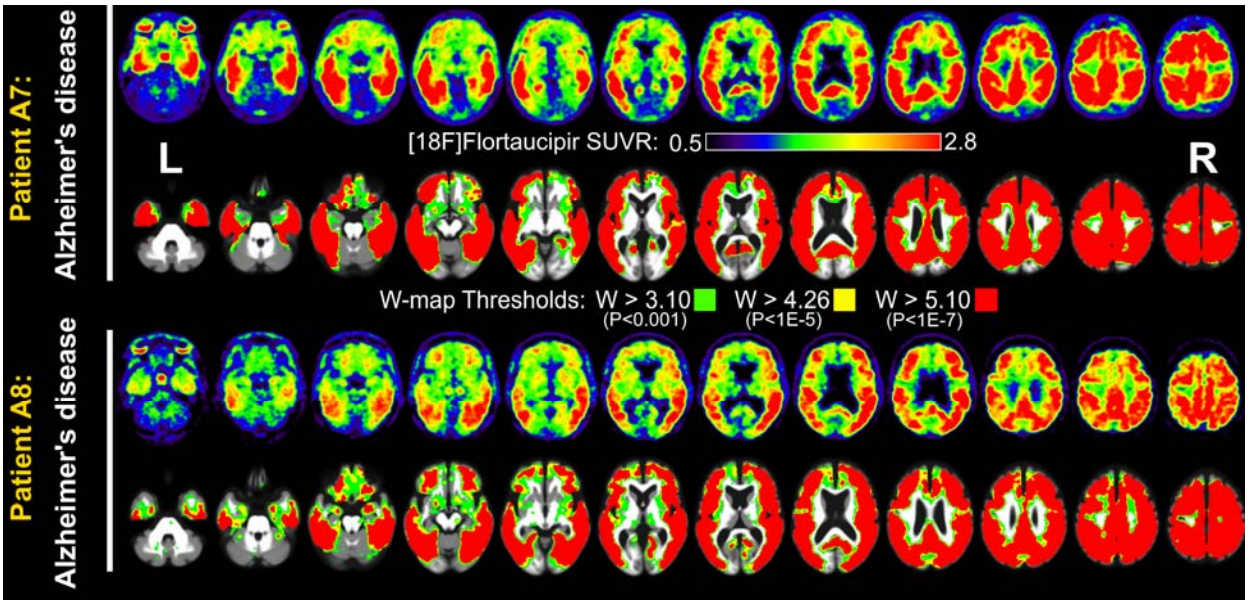
	Middle insula								
	Frontal pole								
	Anterior orbital gyrus								
Subcortical	Ventral striatum								
	Putamen								
	Globus pallidus								
	Subthalamic nucleus								
	Thalamus								
Cerebellum	Cerebellar dentate nucleus								
	Cerebellar folia								
Midbrain	Substantia nigra								
	Tectum								
	Periaqueductal gray								
	Dorsal raphe							**X**	
	Oculomotor nucleus								
	Trochlear nucleus								
Pons	Locus ceruleus							**X**	
	Median raphe								
	Abducens nucleus								
	Facial nucleus								
Medulla	Hypoglossal nucleus								
	Dorsal afferent nucleus, vagus								
	Nucleus solitary tract								
	Olive								

Supplementary Figures

Supplementary Figure 1: FTP-PET SUVR and W-score map images in patients with Alzheimer's disease autopsy diagnosis

(See next page)

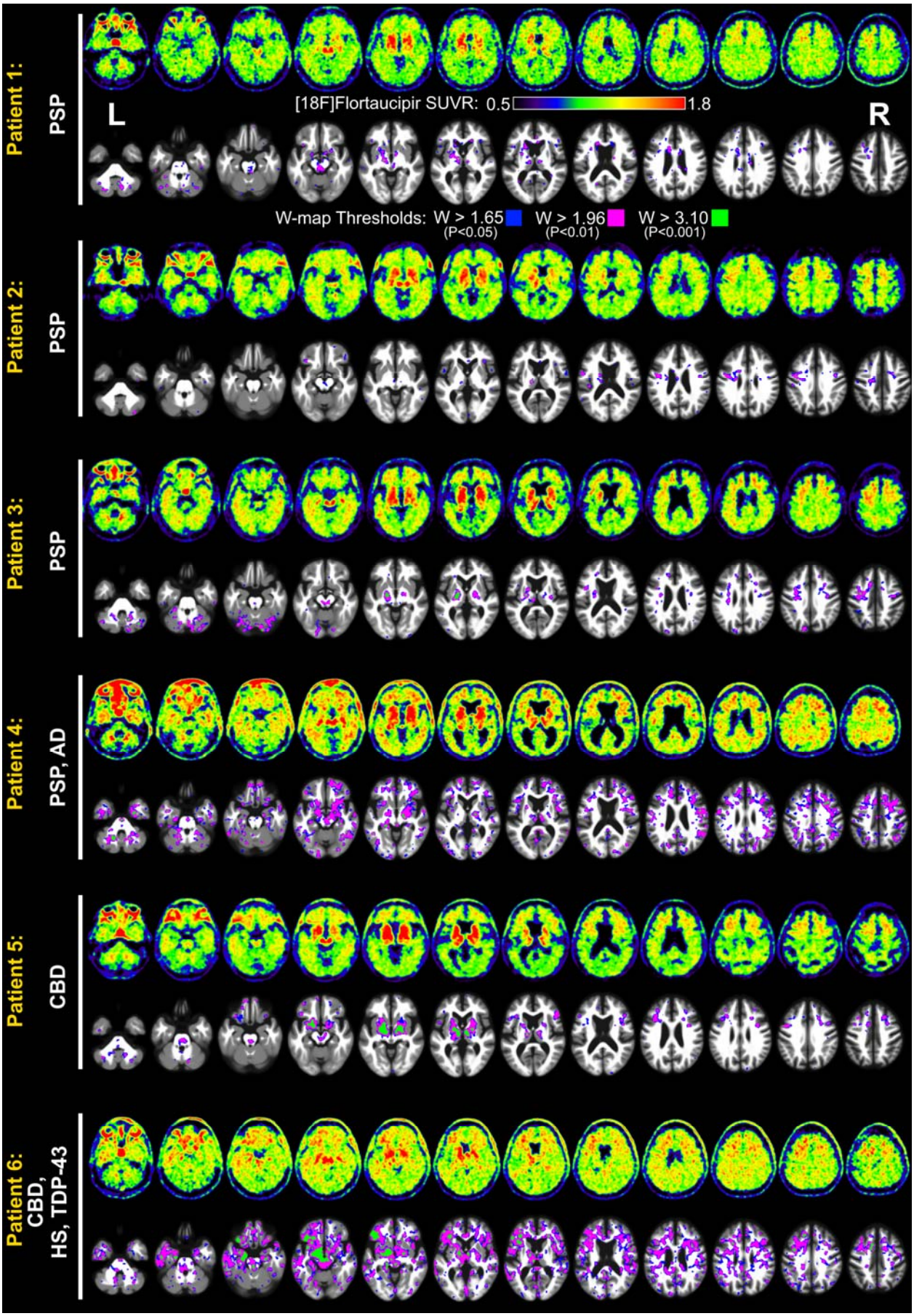

Patient A1:
Alzheimer's disease,
Lewy body disease
[18F]Flortaucipir SUVR: 0.5
2.8
L
R
W-map Thresholds: W > 3.10 (P<0.001)
W > 4.26 (P<1E-5)
W > 5.10 (P<1E-7)
Patient A2:
Alzheimer's disease,
Lewy body disease
Patient A3:
Alzheimer's disease,
Lewy body disease
Patient A4:
Alzheimer's disease
Patient A5:
Alzheimer's disease
Patient A6:
Alzheimer's disease

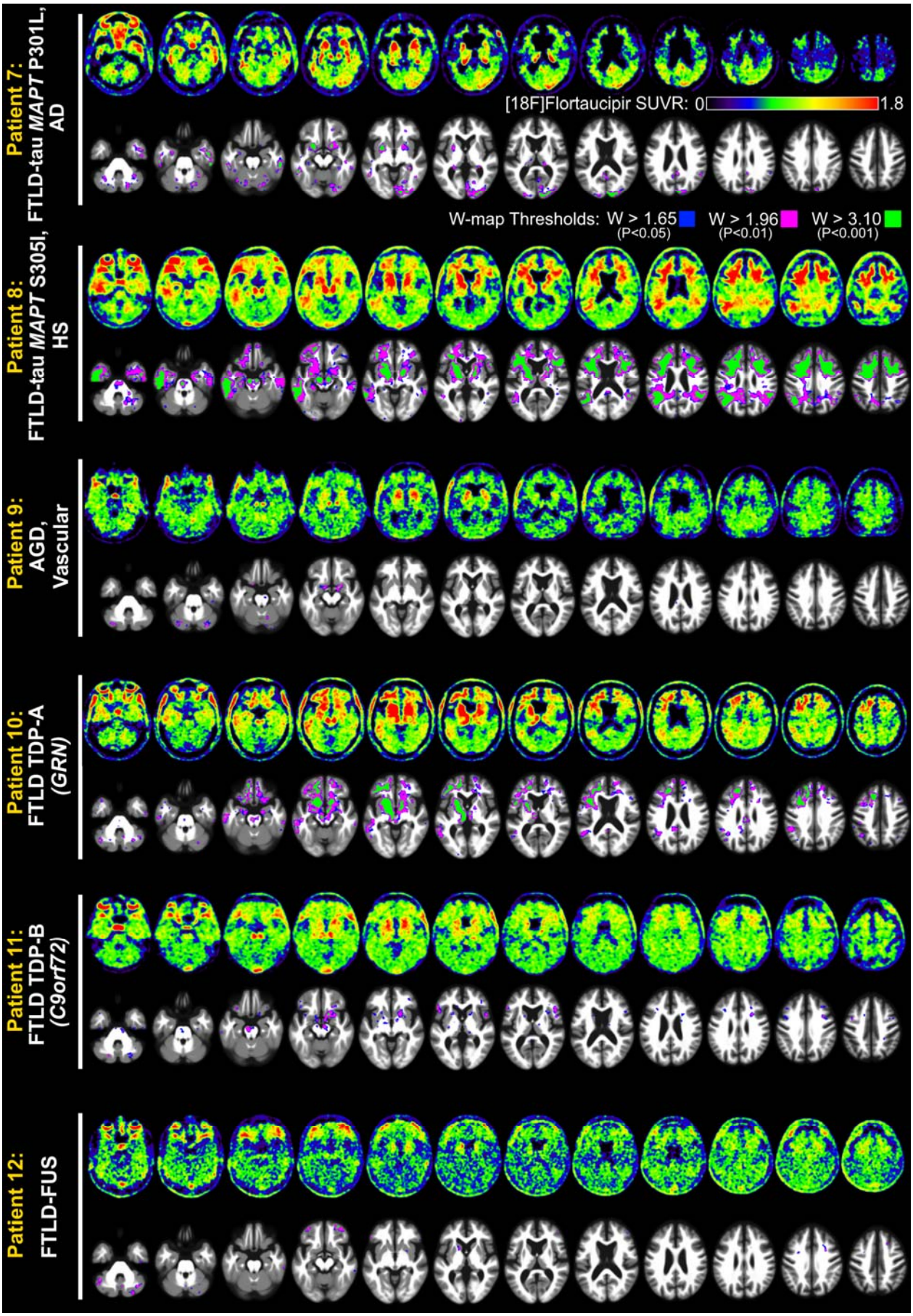


SUVR and W-map images are shown for patients with primary Alzheimer's disease autopsy diagnosis. W-maps highlight areas of increased tracer retention compared to cognitively normal, amyloid-negative controls, adjusting for age as a covariate. Patients with primary Alzheimer's disease pathology had high FTP uptake, and SUVR and W-map thresholds were chosen to highlight the full range of tracer retention in these patients.

Supplementary Figure 2: FTP-PET SUVR and W-score map images in patients with autopsy diagnoses of non-Alzheimer tauopathies, FTLD-TDP, and FTLD-FUS

(See next page)

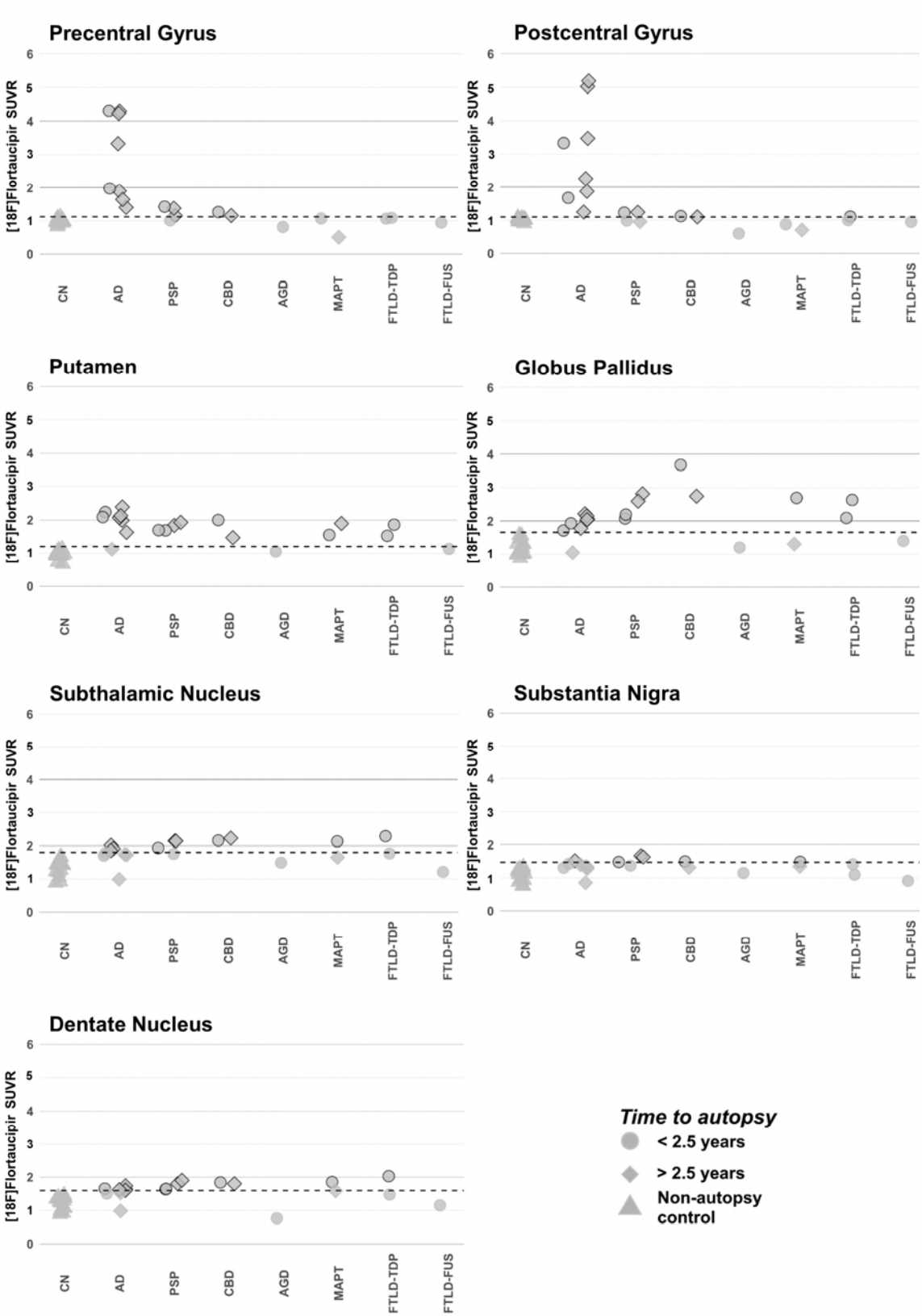

Patient 1:
PSP
L
[18F]Flortaucipir SUVR: 0.5
1.8
R
W-map Thresholds: W > 1.65 (P<0.05)
W > 1.96 (P<0.01)
W > 3.10 (P<0.001)
Patient 2:
PSP
Patient 3:
PSP
Patient 4:
PSP, AD
Patient 5:
CBD
Patient 6:
CBD,
HS, TDP-43


Patient 7:
FTLD-tau MAPT P301L, AD
[18F]Flortaucipir SUVR: 0
1.8
W-map Thresholds: W > 1.65 (P<0.05)
W > 1.96 (P<0.01)
W > 3.10 (P<0.001)
Patient 8:
FTLD-tau MAPT S305I, HS
Patient 9:
AGD, Vascular
Patient 10:
FTLD TDP-A (GRN)
Patient 11:
FTLD TDP-B (C9orf72)
Patient 12:
FTLD-FUS

SUVR and W-map images are shown for patients with primary autopsy diagnoses of non-Alzheimer tauopathies, FTLD-TDP, and FTLD-FUS. These patients had lower FTP uptake than patients with primary Alzheimer's disease autopsy diagnosis, and lower SUVR and W-map thresholds needed to be used to highlight the areas of tracer retention in these patients. The W-map upper threshold (W > 3.10) is the same as the lower threshold used in patients with primary Alzheimer's disease pathology. AD = Alzheimer's disease; AGD = Argyrophilic Grain Disease; CBD = Corticobasal Degeneration; HS = Hippocampal Sclerosis; PSP = Progressive Supranuclear Palsy.

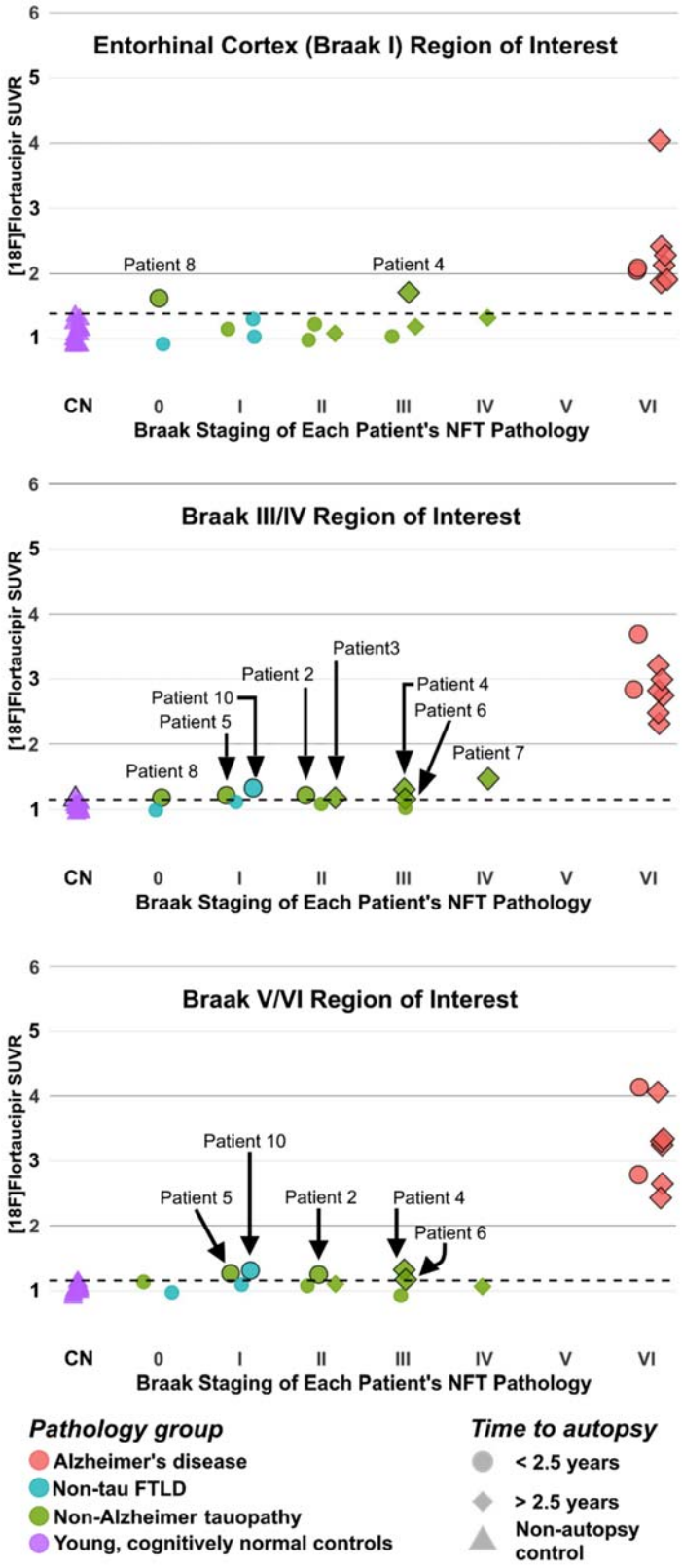
Supplementary Figure 3: FTP-PET SUVR quantification at precentral gyrus, postcentral gyrus, and subcortical regions of interest with partial volume corrected data

(See next page)


Precentral Gyrus
Postcentral Gyrus
Putamen
Globus Pallidus
Subthalamic Nucleus
Substantia Nigra
Dentate Nucleus
[18F]Flortaucipir SUVR
0
1
2
3
4
5
6
CN
AD
PSP
CBD
AGD
MAPT
FTLD-TDP
FTLD-FUS
Time to autopsy
< 2.5 years
> 2.5 years
Non-autopsy control

SUVR quantification, corrected for partial volume effects, was performed at precentral gyrus, postcentral gyrus, putamen, globus pallidus, subthalamic nucleus, substantia nigra, and dentate nucleus regions of interest. Each patient is represented by a single point and coded by time from PET-to-autopsy (shape) and primary neuropathological diagnosis (X-axis). The dotted line represents the threshold for significance, which is calculated from the mean SUVR plus two standard deviations for the young, cognitively normal (CN), non-autopsy controls. Points crossing the significance threshold are highlighted with a black halo. Please note that the range of SUVR values is different for the partial volume corrected data compared to the uncorrected data.

Supplementary Figure 4: FTP-PET SUVR quantification of Braak stage regions of interest with partial volume corrected data



SUVR quantification, corrected for partial volume effects, was performed at entorhinal cortex (Braak I), Braak III/IV, and Braak V/VI regions of interest. Each patient is represented by a single point and coded by their primary autopsy diagnosis (color), time from PET-to-autopsy (shape), and Braak neurofibrillary tangle stage (X-axis). The dotted line represents the threshold for significance, which is calculated from the mean SUVR plus two standard deviations for the young, cognitively normal (CN), non-autopsy controls. Points crossing the significance threshold are highlighted with a black halo. Please note that the range of SUVR values is different for the partial volume corrected data compared to the uncorrected data.

Supplementary References

Ashburner J, Friston KJ. Unified segmentation. NeuroImage 2005; 26: 839–51.

Baker SL, Harrison TM, Maaß A, La Joie R, Jagust W. Effect of off-target binding on 18F-Flortaucipir variability in healthy controls across the lifespan. J Nucl Med Off Publ Soc Nucl Med 2019.

Choi JY, Cho H, Ahn SJ, Lee JH, Ryu YH, Lee MS, et al. Off-Target 18F-AV-1451 Binding in the Basal Ganglia Correlates with Age-Related Iron Accumulation. J Nucl Med Off Publ Soc Nucl Med 2018; 59: 117–20.

Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. NeuroImage 2006; 31: 968–80.

Diedrichsen J, Balsters JH, Flavell J, Cussans E, Ramnani N. A probabilistic MR atlas of the human cerebellum. Neuroimage 2009; 46: 39–46.

Diedrichsen J, Maderwald S, Küper M, Thürling M, Rabe K, Gizewski ER, et al. Imaging the deep cerebellar nuclei: A probabilistic atlas and normalization procedure. Neuroimage 2011; 54: 1786–94.

Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, et al. Whole brain segmentation: Automated labeling of neuroanatomical structures in the human brain. Neuron 2002; 33: 341–55.

Harrison TM, La Joie R, Maass A, Baker SL, Swinnerton K, Fenton L, et al. Longitudinal tau accumulation and atrophy in aging and alzheimer disease. Ann Neurol 2019; 85: 229–40.

Klunk WE, Koeppe RA, Price JC, Benzinger TL, Devous MD, Jagust WJ, et al. The Centiloid Project: standardizing quantitative amyloid plaque estimation by PET. Alzheimers Dement J Alzheimers Assoc 2015; 11: 1-15.e1–4.

La Joie R, Ayakta N, Seeley WW, Borys E, Boxer AL, DeCarli C, et al. Multisite study of the relationships between antemortem [11C]PIB-PET Centiloid values and postmortem measures of Alzheimer's disease neuropathology. Alzheimers Dement J Alzheimers Assoc 2019; 15: 205–16.

La Joie R, Bejanin A, Fagan AM, Ayakta N, Baker SL, Bourakova V, et al. Associations between [18F]AV1451 tau PET and CSF measures of tau pathology in a clinical sample. Neurology 2018; 90: e282–90.

Landau SM, Lu M, Joshi AD, Pontecorvo M, Mintun MA, Trojanowski JQ, et al. Comparing positron emission tomography imaging and cerebrospinal fluid measurements of β-amyloid. Ann Neurol 2013; 74: 826–36.

Lesman-Segev OH, La Joie R, Stephens ML, Sonni I, Tsai R, Bourakova V, et al. Tau PET and multimodal brain imaging in patients at risk for chronic traumatic encephalopathy. NeuroImage Clin 2019; 24.

Maass A, Landau S, Baker SL, Horng A, Lockhart SN, La Joie R, et al. Comparison of multiple tau-PET measures as biomarkers in aging and Alzheimer's disease. NeuroImage 2017; 157: 448–63.

Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. Neuroimage 2003; 19: 1233–9.

Villeneuve S, Rabinovici GD, Cohn-Sheehy BI, Madison C, Ayakta N, Ghosh PM, et al. Existing Pittsburgh Compound-B positron emission tomography thresholds are too high: statistical and pathological evaluation. Brain J Neurol 2015; 138: 2020–33.