

Supplementary data

Characterisation of tau PET tracer [¹⁸F]AV-1451 binding to *post-mortem* tissue in Alzheimer's disease, primary tauopathies and other dementias

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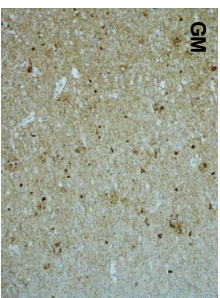
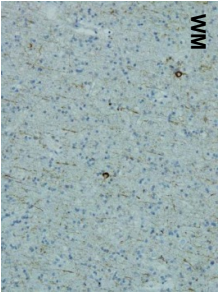
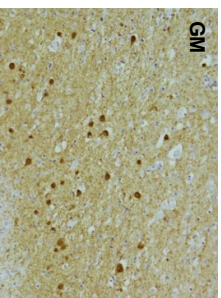
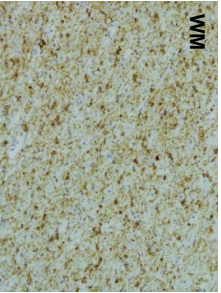
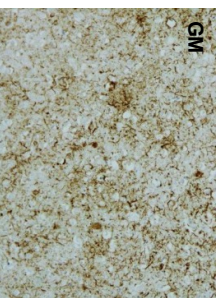
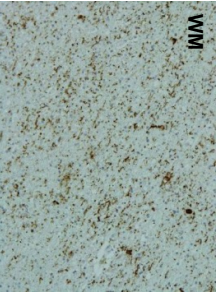
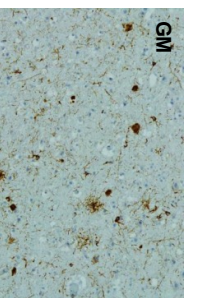
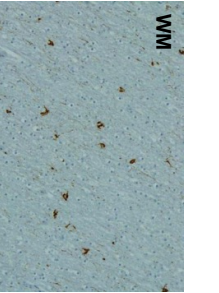
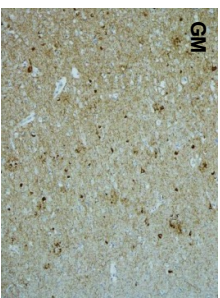
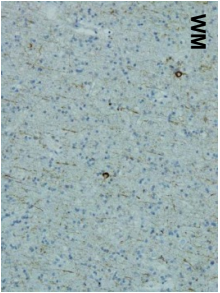
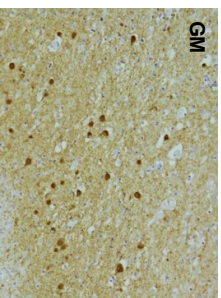
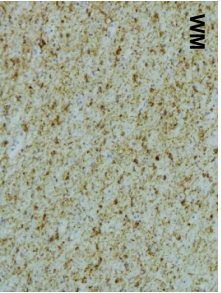
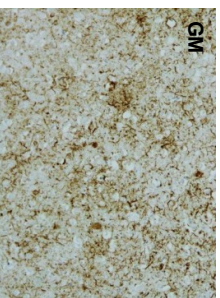
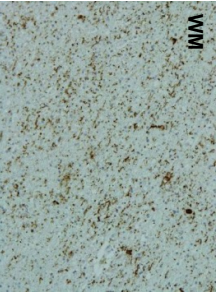
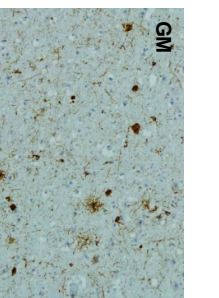
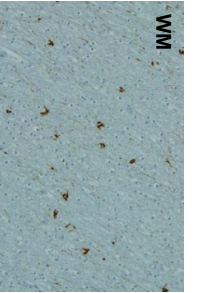
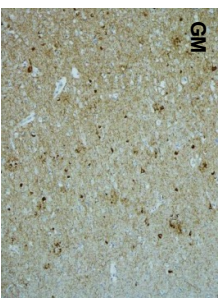
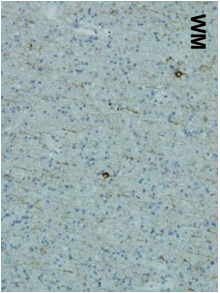
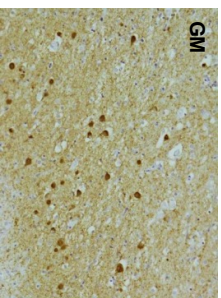
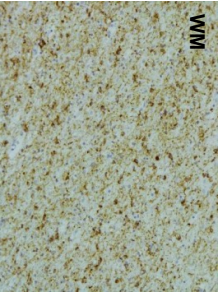
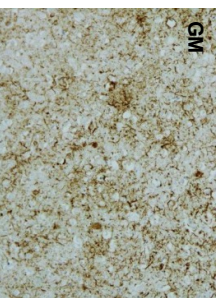
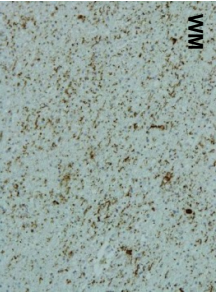
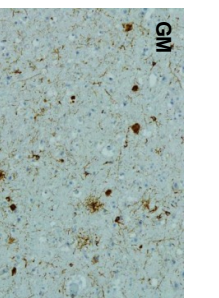
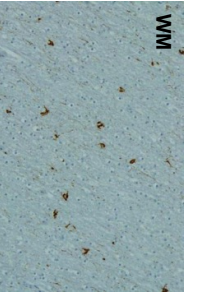
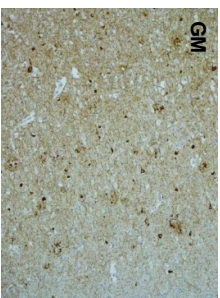
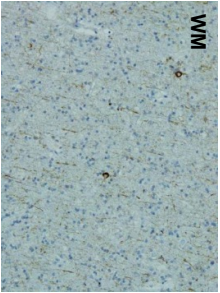
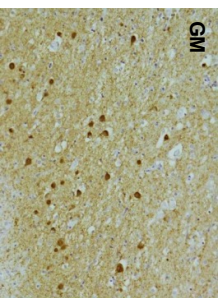
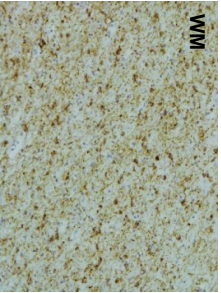
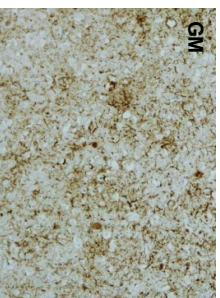
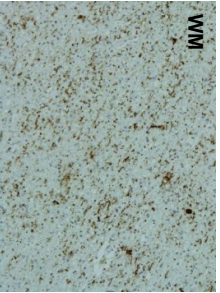
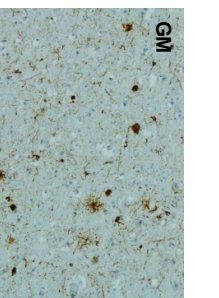
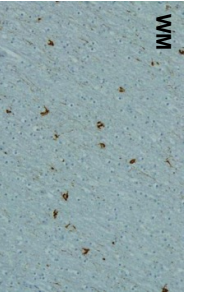
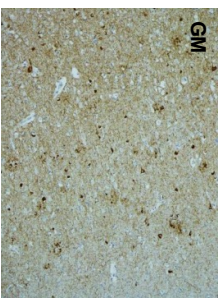
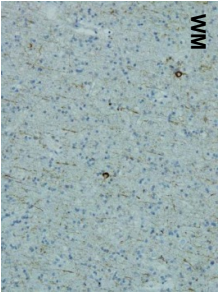
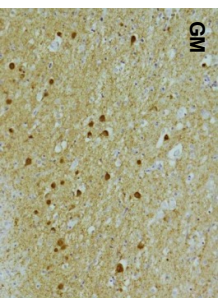
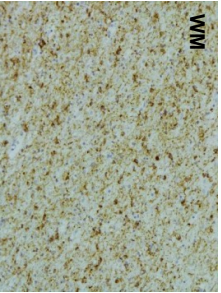
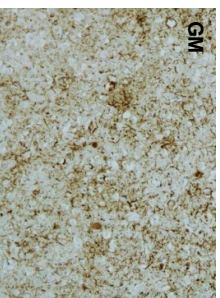
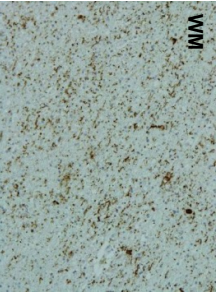
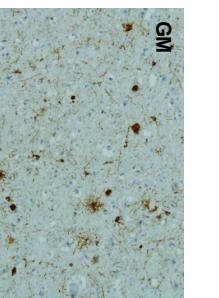
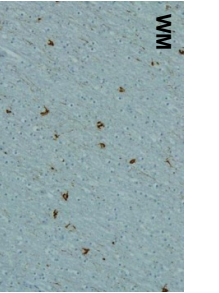
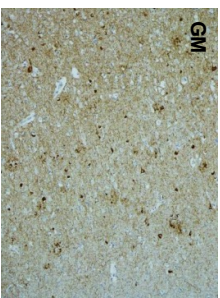
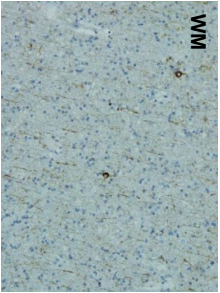
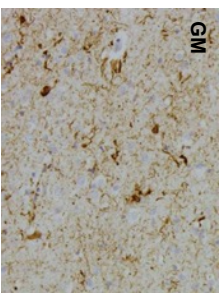
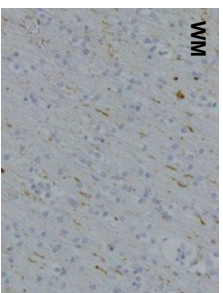
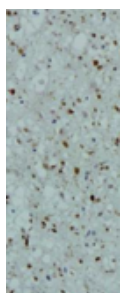

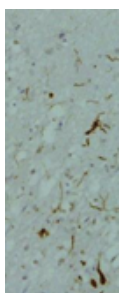
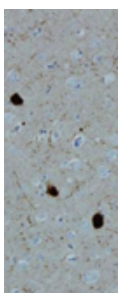

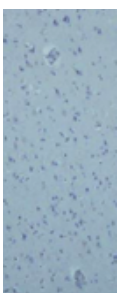
Pathological diagnosis [†]	Clinical diagnosis [†]	Gender	Age at onset	Age at death	Duration (years)	Immunohistochemistry [‡]	
AD	PICK	F	50	66	16		
	AD	M	69	81	12		
	VD	M	62	72	10		
	AD	F	70	86	16		
PICK	AD (PCA)	M	55	56	10		
	bvFTD	M	57	62	5		
	<i>n.d.</i>	M	63	75	12		
	SD	M	55	72	17		
	<i>n.d.</i>	M	70	78	8		
	<i>n.d.</i>	M	53	67	14		
CBD	PNFA	M	57	67	10		
	PSP	F	62	69	7		
	CBD	F	62	68	6		
	CBS	M	69	77	8		
PSP	CBS	F	67	77	10		
	PSP	M	67	73	6		
	PSP-1	M	62	74	12		
PSP-2	Stable cognitive impairment following cerebral vasculitis	M	62	74	12		
	Atypical parkinsonism, possible CBD/PSP overlap	F	60	68	8		
	PSP	F	65	74	9		
PSP	PSP	F	70	76	6		

Table S 1, continued. Case demographics and characteristic pathological lesions observed in the selected cases *

Pathological diagnosis †	Clinical diagnosis †	Gender	Age at onset	Age at death	Duration (years)	Immunohistochemistry ‡
FTDP-17	<i>n.d.</i>	M	54	58	4	
	bvFTD – MAPT R406W	M	55	66	11	
	bvFTD – MAPT 10+16	M	59	66	7	
FTLD-TDPA	bvFTD – MAPT 10+16	M	45	51	6	
	bvFTD	M	62	72	10	
	bvFTD	F	57	63	6	
FTLD-TDPC	PNFA	F	57	62	5	
	SD	M	50	65	15	
	SD	M	64	74	10	
DLB/PDD	SD	M	64	78	14	
	PD with dementia	F	57	81	24	
	PD	F	57	83	26	
Normal	PD	F	72	92	20	
	<i>n.a.</i>	F	<i>n.a.</i>	80	<i>n.a.</i>	
	<i>n.a.</i>	M	<i>n.a.</i>	38	<i>n.a.</i>	
<i>n.a.</i>	F	<i>n.a.</i>	86	<i>n.a.</i>		
<i>n.a.</i>	M	<i>n.a.</i>	89	<i>n.a.</i>		

* **Abbreviations:** AD, Alzheimer’s disease; PICK, Pick’s disease; CBD, corticobasal degeneration; PSP, progressive supranuclear palsy; FTDP-17, frontotemporal dementia with parkinsonism linked to chromosome 17 (microtubule-associated protein tau mutation); FTLD-TDPA/C, frontotemporal lobar degeneration linked to TAR DNA-binding protein-43, type A/C; DLB/PDD, dementia with Lewy bodies/Parkinson’s disease with dementia; VD, vascular dementia; PCA, posterior cortical atrophy; bvFTD, behavioural variant frontotemporal dementia; SD, semantic dementia; PNFA, progressive nonfluent aphasia; CBS, corticobasal syndrome; PD, Parkinson’s disease; F,

female; M, male; GM, grey matter; WM, white matter; *n.d.*, not diagnosed (these cases have not been diagnosed and treated at the UCL Dementia Research Centre but brains have been donated to the Queen Square Brain Bank from elsewhere); *n.a.*, not applicable.

† ***Pathological and clinical diagnosis*** were made at autopsy (*post-mortem*) and after first clinical presentation, respectively. The case that is printed in bold in the “Clinical diagnosis” column is the one shown under “Immunohistochemistry”.

‡ ***Tau immunohistochemistry*** demonstrated abundant neurofibrillary tangles (NFTs), plaque-associated neurites and neuropil threads in AD in the GM with occasional coiled bodies and threads in the WM. Characteristic compact, rounded neuronal cytoplasmic inclusions (Pick bodies), ramified astrocytes and fine neuropil threads were present in the PICK cases in the GM with a dense network of tau positive threads and tau-immunoreactive oligodendroglia in the WM. Tufted astrocytes, NFTs and neuropil threads were seen in the GM in PSP, while the WM contained numerous coiled bodies and fine tau-positive threads. Numerous neuropil threads and astrocytic plaques were detected in the GM in CBD, whereas a dense network of tau-positive threads was present in the WM. The FTDP-17 case displayed had a R406W MAPT mutation; NFTs and threads were detected in the GM, whereas the WM showed long neuropil threads. FTLD-TDPA cases showed cytoplasmic inclusions and short threads, while FTLD-TDPC cases exhibited long corkscrew-shaped neurites. Cortical Lewy bodies and numerous fine α -synuclein-positive neurites were seen in the frontal cortex of dementia with DLB/PDD cases. No tau immunoreactive structures were seen in the cerebral cortex of the normal control cases. All images x20 objective.

Table S 2. Quantification of AT8 staining and [¹⁸F]AV-1451 binding to tau in flash frozen *post-mortem* brain sections *

	Frontal cortex			Temporal cortex, cerebellum (PSP), parietal cortex (CBD)			
	AT8 IHC Tau load (%)	Phosphorimaging with [¹⁸ F]AV-1451 TB (kBq/cm ²)	NSB (kBq/cm ²)	AT8 IHC Tau load (%)	Phosphorimaging with [¹⁸ F]AV-1451 TB (kBq/cm ²)	NSB (kBq/cm ²)	SB (kBq/cm ²)
AD	3.0	4.6±1.1	1.3±0.4	2.1	5.5±0.7	1.3±0.4	4.2±0.5
PICK	0.8	3.0±0.6	1.1±0.3	0.7	2.8±0.3	1.1±0.3	1.7±0.5
CBD	1.1	1.3±0.4	0.5±0.1	1.0	1.3±0.5	0.5±0.1	0.8±0.4
PSP	0.9	1.2±0.5	0.4±0.2	0.4	1.3±0.6	0.5±0.3	0.8±0.5
FTDP-17	0.5	2.9±0.9	0.9±0.3	0.5	3.0±1.1	0.9±0.5	2.1±0.8
FTLD-TDPA	0	1.9±0.8	0.7±0.4	-	1.5±0.5	0.6±0.3	0.9±0.2
FTLD-TDPC	0	2.2±0.9	0.8±0.4	-	1.7±0.4	0.6±0.2	1.1±0.2
DLB/PDD	0	1.2±0.3	0.5±0.1	-	1.2±0.3	0.4±0.1	0.8±0.2
Controls	0	1.7±0.4	0.6±0.1	-	1.6±0.2	0.5±0.0	1.1±0.3

* *Abbreviations*: AD, Alzheimer's disease; PICK, Pick's disease; CBD, corticobasal degeneration; PSP, progressive supranuclear palsy; FTDP-17, frontotemporal dementia with parkinsonism linked to chromosome 17; FTLD-TDPA/C, frontotemporal lobar degeneration linked to TAR DNA-binding protein-43, type A/C; DLB/PDD, dementia with Lewy bodies/Parkinson's disease with dementia; IHC, immunohistochemistry; TB, total binding; NSB, non-specific binding; SB, specific binding.

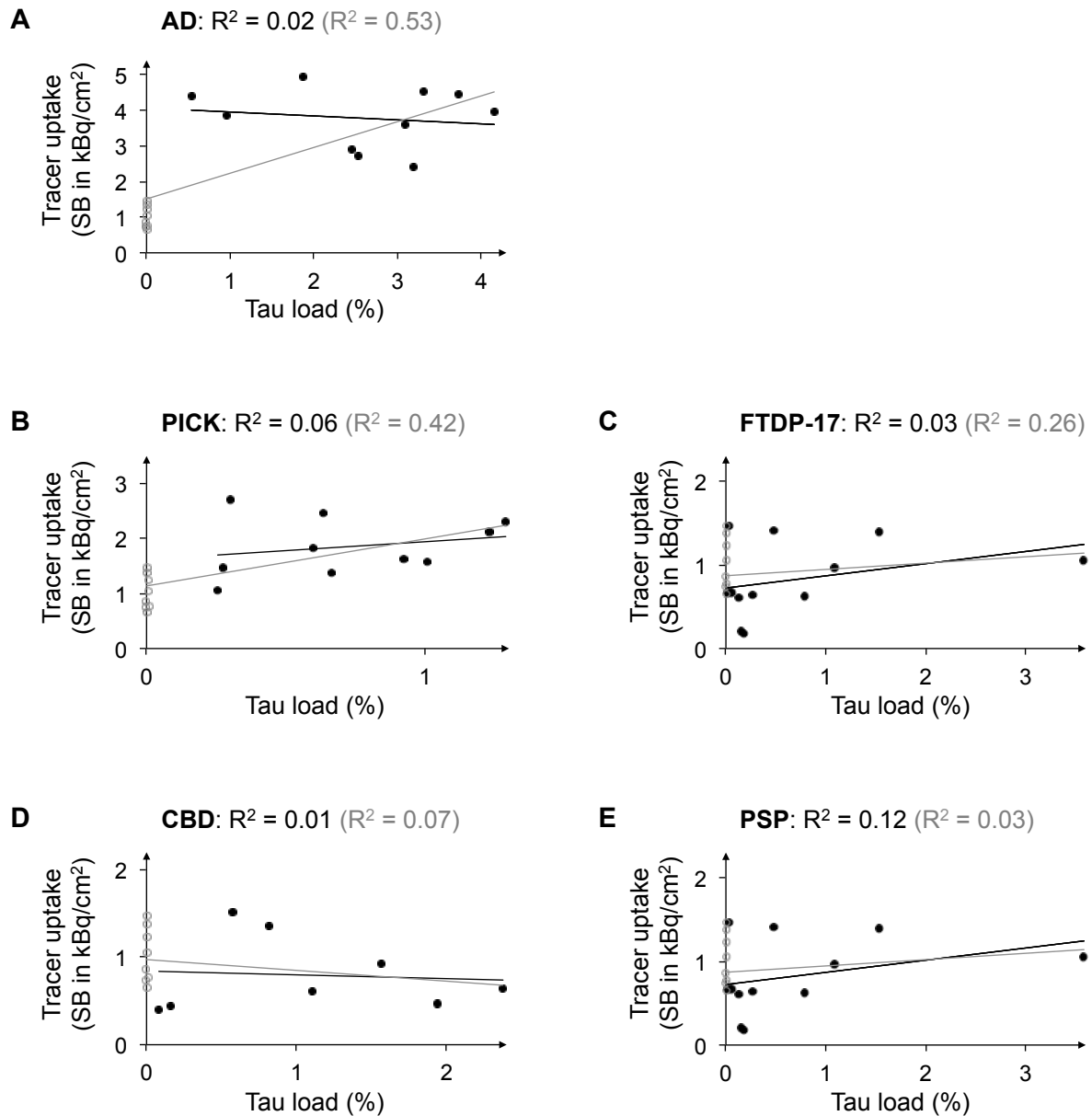


Figure S 1. Correlation of the specific binding of [^{18}F]AV-1451 in tauopathies (closed black dots) and control cases (open grey circles) with tau load as determined by AT8 staining in adjacent sections. R^2 values without (black) and with (grey) control cases included. *Abbreviations:* AD, Alzheimer’s disease; FTDP-17, frontotemporal dementia with parkinsonism linked to chromosome 17 (caused by a mutation of the microtubule-associated protein tau (MAPT) gene); PICK, Pick’s disease; CBD, corticobasal degeneration; PSP, progressive supranuclear palsy.