

## Supplementary Material

**Supplementary Table 1. Demographics, genetic and clinical features for each patient.**

Pt	Gene	Diagnosis	Sex	Age at PET	Age at Diagnosis	Age at Onset	Disease duration at PET	Years of Education	ACE-R /100
A	MAPT	bvFTD	F	51	51	46	5.5	16	43
B	MAPT	bvFTD	F	61	60	52	9	16	44
C	GRN	bvFTD	F	71	70	66	4.8	10	33
D	GRN	nfPPA	M	66	65	63	2.4	10	76
E	C9orf72	bvFTD	M	56	56	54	2.8	10	53
F	C9orf72	bvFTD	F	51	51	47	4.5	10	41
G	C9orf72	bvFTD	M	59	58	56	3	9	46

Abbreviations: Pt=patient; bvFTD=behavioural variant frontotemporal dementia; nfPPA=non-fluent primary progressive aphasia; F=Female; M=Male; ACE-R= Addenbrooke's Cognitive Examination Revised

**Supplementary Table 2. Demographics of the two age- and sex-matched control groups compared to each patient in radioligand-specific tests. Age, years of education, and ACE-R scores were compared between the two groups of controls with independent-samples t-tests, while sex was compared with the Chi-square test.**

Group control	N	Sex (F/M)	Age (mean $\pm$ SD)	Education (mean $\pm$ SD)	ACE-R (mean $\pm$ SD)
[ <sup>11</sup> C]PK11195	15	8/7	68.8 $\pm$ 5.5	14.4 $\pm$ 2.8	93.3 $\pm$ 4.4
[ <sup>18</sup> F]AV-1451	15	7/8	67.3 $\pm$ 7.6	15.5 $\pm$ 2.3	95.7 $\pm$ 3.2
Difference controls (p-value)	-	0.72	0.56	0.26	0.11

Abbreviations: F/M= female/male; SD=standard deviation; ACE-R= Addenbrooke's Cognitive Examination Revised

**Supplementary Table 3. [<sup>11</sup>C]PK11195 binding potential (BP<sub>ND</sub>) values and Z-scores (Z) for brain regions with statistically significant increased BP<sub>ND</sub> in each patient (Pt) compared to controls at p < 0.05 uncorrected (tests surviving FDR correction are in bold). Mean and standard deviation (SD) BP<sub>ND</sub> values for controls are also reported.**

Region		Controls BP <sub>ND</sub>		Pt A		Pt B		Pt C		Pt D		Pt E		Pt F		Pt G	
Name	#	Mean	SD	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z
Hippocampus R	1	0.01	0.07	0.28	<b>3.81</b>	-	-	-	-	-	-	-	-	-	-	-	-
Hippocampus L	2	0.04	0.07	-	-	0.29	<b>3.75</b>	-	-	-	-	-	-	-	-	-	-
Amygdala R	3	0.01	0.07	0.37	<b>4.95</b>	0.21	2.72	-	-	-	-	0.22	2.87	-	-	-	-
Amygdala L	4	0.06	0.04	0.34	<b>6.35</b>	0.34	<b>6.40</b>	-	-	-	-	-	-	-	-	-	-
Anterior temporal lobe medial part R	5	0.04	0.06	0.23	<b>3.11</b>	-	-	-	-	-	-	0.35	<b>5.10</b>	0.19	2.50	-	-
Anterior temporal lobe medial part L	6	0.04	0.06	0.25	<b>3.14</b>	0.22	2.68	-	-	-	-	-	-	-	-	-	-
Anterior temporal lobe lateral part R	7	0.10	0.07	0.26	2.42	0.33	<b>3.46</b>	-	-	-	-	-	-	-	-	-	-
Anterior temporal lobe lateral part L	8	0.03	0.05	0.27	<b>4.70</b>	0.26	<b>4.38</b>	-	-	-	-	0.19	3.11	0.27	<b>4.70</b>	-	-
Parahippocampal and ambient gyri R	9	0.05	0.05	0.27	<b>4.08</b>	0.19	2.56	-	-	-	-	0.22	3.05	-	-	-	-
Parahippocampal and ambient gyri L	10	0.07	0.05	0.28	<b>3.79</b>	0.41	<b>6.23</b>	-	-	-	-	0.22	2.73	-	-	-	-
Middle and inferior temporal gyrus R	13	0.01	0.04	-	-	0.14	<b>3.32</b>	-	-	0.11	2.56	-	-	-	-	-	-
Middle and inferior temporal gyrus L	14	-0.02	0.03	0.14	<b>6.02</b>	0.08	<b>3.77</b>	0.08	<b>3.70</b>	-	-	0.08	<b>3.95</b>	0.10	<b>4.50</b>	-	-
Fusiform gyrus R	15	-0.01	0.02	0.11	<b>5.07</b>	0.20	<b>9.27</b>	0.05	2.41	0.19	<b>8.68</b>	0.16	<b>7.42</b>	0.09	<b>4.14</b>	-	-
Fusiform gyrus L	16	-0.01	0.05	0.16	<b>3.36</b>	0.24	<b>4.84</b>	-	-	0.10	2.21	0.37	<b>7.33</b>	-	-	0.11	2.37
Insula L	20	0.02	0.05	-	-	-	-	-	-	-	-	0.16	2.92	-	-	-	-
Middle frontal gyrus L	28	-0.05	0.06	-	-	-	-	-	-	-	-	-	-	0.09	2.28	-	-
Middle frontal gyrus R	29	-0.01	0.05	-	-	0.08	1.84	-	-	-	-	-	-	0.11	2.63	-	-
Nucleus accumbens L	36	0.11	0.07	-	-	0.33	<b>3.06</b>	-	-	-	-	-	-	-	-	-	-
Nucleus accumbens R	37	0.08	0.08	0.45	<b>4.84</b>	-	-	-	-	-	-	-	-	-	-	-	-
Putamen L	38	0.06	0.05	-	-	-	-	0.29	<b>4.85</b>	0.16	1.98	-	-	-	-	-	-
Putamen R	39	0.08	0.04	0.15	1.83	0.18	2.59	0.19	3.07	0.15	1.98	-	-	-	-	-	-
Pallidum L	42	0.03	0.10	0.27	2.40	-	-	0.25	2.13	-	-	-	-	0.27	2.40	-	-
Straight gyrus L	52	0.18	0.07	0.43	<b>3.55</b>	-	-	-	-	-	-	-	-	-	-	-	-
Straight gyrus R	53	0.16	0.09	0.44	<b>3.20</b>	-	-	-	-	-	-	-	-	-	-	-	-
Anterior orbital gyrus L	54	0.04	0.06	-	-	-	-	-	-	-	-	-	-	0.37	<b>5.27</b>	-	-
Anterior orbital gyrus R	55	0.07	0.06	-	-	-	-	-	-	-	-	-	-	0.27	<b>3.15</b>	0.23	2.56
Inferior frontal gyrus L	56	0.09	0.05	-	-	-	-	-	-	-	-	-	-	0.23	2.83	-	-
Inferior frontal gyrus R	57	0.12	0.06	-	-	0.25	2.31	-	-	-	-	-	-	0.23	2.03	-	-
Superior frontal gyrus L	58	0.07	0.05	-	-	-	-	-	-	-	-	-	-	-	-	0.18	2.48
Superior frontal gyrus R	59	0.04	0.06	-	-	-	-	-	-	-	-	-	-	-	-	0.17	2.11

Lingual gyrus L	64	0.15	0.07	-	-	-	-	-	-	-	-	-	-	-	-	0.29	2.10
Lingual gyrus R	65	0.11	0.06	-	-	-	-	-	-	-	-	-	-	-	-	0.23	1.96
Cuneus L	66	0.17	0.05	-	-	-	-	-	-	-	-	-	-	0.35	<b>3.74</b>	0.27	2.12
Cuneus R	67	0.12	0.05	-	-	-	-	-	-	-	-	-	-	-	-	0.23	1.88
Medial orbital gyrus L	68	0.12	0.06	0.25	1.97	-	-	-	-	-	-	-	-	0.36	<b>3.82</b>	-	-
Lateral orbital gyrus L	70	0.13	0.06	-	-	-	-	0.28	2.42	-	-	-	-	0.52	<b>6.22</b>	-	-
Lateral orbital gyrus R	71	0.13	0.06	-	-	-	-	-	-	-	-	-	-	0.52	<b>6.27</b>	-	-
Posterior orbital gyrus L	72	0.10	0.07	0.29	2.55	-	-	-	-	-	-	-	-	-	-	-	-
Posterior orbital gyrus R	73	0.14	0.06	-	-	-	-	-	-	-	-	-	-	0.27	2.32	-	-
Substantia nigra L	74	0.22	0.07	-	-	-	-	-	-	-	-	-	-	0.44	2.91	-	-
Substantia nigra R	75	0.15	0.07	-	-	-	-	0.60	<b>6.47</b>	-	-	-	-	-	-	-	-
Subgenual frontal cortex L	76	0.01	0.07	0.30	<b>4.13</b>	-	-	-	-	-	-	-	-	-	-	-	-
Subcallosal area L	78	0.17	0.12	-	-	-	-	-	-	-	-	0.43	2.10	-	-	-	-
Subcallosal area R	79	0.23	0.16	-	-	-	-	0.68	2.91	-	-	-	-	-	-	-	-
Presubgenual frontal cortex L	80	0.15	0.10	0.35	1.87	-	-	-	-	-	-	-	-	-	-	-	-
Presubgenual frontal cortex R	81	0.10	0.08	0.25	1.83	-	-	-	-	-	-	-	-	-	-	-	-
Superior temporal gyrus anterior part L	82	0.09	0.09	0.32	2.53	-	-	-	-	-	-	-	-	-	-	-	-
Superior temporal gyrus anterior part R	83	0.11	0.10	0.29	1.93	0.30	1.99	-	-	-	-	0.35	2.48	-	-	-	-

Abbreviations: L=Left; R=Right

**Supplementary Table 4. [<sup>18</sup>F]AV1451 binding potential (BP<sub>ND</sub>) values and Z-scores (Z) for brain regions with statistically significant increased BP<sub>ND</sub> in each patient (Pt) compared to controls at  $p < 0.05$  uncorrected (tests surviving FDR correction are in bold). Mean and standard deviation (SD) BP<sub>ND</sub> values for controls are also reported.**

Region		Controls BP <sub>ND</sub>		Pt A		Pt B		Pt C		Pt D		Pt E		Pt F		Pt G	
Name	#	Mean	SD	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z	BP <sub>ND</sub>	Z
Hippocampus L	2	0.07	0.08	-	-	-	-	0.34	3.12	-	-	-	-	-	-	-	-
Amygdala R	3	0.06	0.07	0.35	<b>4.11</b>	-	-	-	-	-	-	-	-	-	-	-	-
Amygdala L	4	0.05	0.08	0.24	<b>2.51</b>	-	-	-	-	-	-	-	-	-	-	-	-
Anterior temporal lobe medial part R	5	0.00	0.06	0.25	<b>4.39</b>	0.14	2.42	-	-	-	-	0.15	2.59	-	-	-	-
Anterior temporal lobe medial part L	6	0.01	0.06	0.37	<b>6.62</b>	-	-	0.11	1.86	-	-	0.27	<b>4.80</b>	-	-	-	-
Anterior temporal lobe lateral part R	7	0.05	0.08	0.35	<b>3.67</b>	0.24	2.27	-	-	-	-	0.22	2.03	-	-	-	-
Anterior temporal lobe lateral part L	8	0.04	0.08	0.42	<b>4.85</b>	0.21	2.20	-	-	-	-	0.32	<b>3.55</b>	-	-	-	-
Parahippocampal and ambient gyri R	9	0.03	0.06	0.29	<b>4.11</b>	0.16	2.11	-	-	-	-	-	-	-	-	-	-
Parahippocampal and ambient gyri L	10	0.04	0.06	0.27	<b>3.66</b>	0.19	2.37	0.17	2.17	-	-	-	-	-	-	-	-
Middle and inferior temporal gyrus R	13	0.01	0.06	0.16	<b>2.56</b>	0.17	2.68	-	-	-	-	0.12	1.82	-	-	-	-
Middle and inferior temporal gyrus L	14	0.01	0.05	0.29	<b>6.01</b>	0.13	2.67	0.15	3.04	-	-	0.28	<b>5.83</b>	-	-	-	-
Fusiform gyrus R	15	0.02	0.08	0.30	<b>3.63</b>	0.21	2.43	-	-	-	-	-	-	-	-	-	-
Fusiform gyrus L	16	0.03	0.06	0.34	<b>5.60</b>	-	-	-	-	-	-	0.27	<b>4.36</b>	-	-	-	-
Insula L	20	0.02	0.05	0.15	2.41	-	-	-	-	-	-	-	-	-	-	-	-
Lateral remainder of occipital lobe L	22	-0.04	0.06	-	-	0.09	2.04	-	-	-	-	-	-	-	-	-	-
Cingulate gyrus anterior part L	24	0.13	0.06	0.27	2.32	-	-	-	-	-	-	-	-	-	-	-	-
Cingulate gyrus anterior part R	25	0.09	0.05	-	-	0.19	1.84	-	-	-	-	-	-	-	-	-	-
Cingulate gyrus posterior part L	26	0.07	0.05	0.16	1.84	0.18	2.17	-	-	-	-	-	-	-	-	-	-
Cingulate gyrus posterior part R	27	0.05	0.05	0.15	1.91	-	-	-	-	-	-	-	-	-	-	-	-
Middle frontal gyrus L	28	-0.06	0.05	0.06	2.29	0.16	<b>4.22</b>	-	-	-	-	0.07	2.58	-	-	-	-
Middle frontal gyrus R	29	-0.02	0.06	-	-	0.20	3.57	-	-	-	-	-	-	-	-	-	-
Posterior temporal lobe L	30	-0.01	0.06	0.13	2.33	0.13	2.32	-	-	-	-	-	-	-	-	-	-
Posterior temporal lobe R	31	-0.01	0.05	0.09	1.95	0.11	2.48	-	-	-	-	-	-	-	-	-	-
Inferiolateral remainder of parietal lobe L	32	-0.01	0.07	0.13	2.16	0.16	2.69	-	-	-	-	-	-	-	-	-	-
Inferiolateral remainder of parietal lobe R	33	0.01	0.05	-	-	0.16	3.10	-	-	-	-	-	-	-	-	-	-
Caudate nucleus L	34	0.21	0.10	0.40	1.85	-	-	-	-	-	-	-	-	-	-	-	-
Caudate nucleus R	35	0.18	0.11	-	-	0.43	2.34	-	-	-	-	-	-	-	-	-	-
Nucleus accumbens L	36	0.16	0.07	0.62	<b>6.35</b>	0.30	1.99	0.43	3.78	-	-	-	-	-	-	-	-

Nucleus accumbens R	37	0.19	0.12	0.42	1.92	0.42	1.86	-	-	-	-	-	-	-	-	-	-
Putamen L	38	0.26	0.08	-	-	0.40	1.85	-	-	-	-	-	-	-	-	-	-
Thalamus L	40	0.23	0.06	0.34	1.84	-	-	0.39	2.59	-	-	-	-	-	-	-	-
Pallidum L	42	0.18	0.09	0.42	<b>2.64</b>	0.39	2.34	-	-	-	-	0.45	2.97	-	-	-	-
Pallidum R	43	0.21	0.13	-	-	0.47	2.03	-	-	-	-	-	-	-	-	-	-
Straight gyrus L	52	0.15	0.07	0.50	<b>4.72</b>	-	-	-	-	-	-	-	-	-	-	-	-
Straight gyrus R	53	0.13	0.07	0.38	<b>3.68</b>	-	-	-	-	-	-	-	-	-	-	-	-
Anterior orbital gyrus L	54	0.01	0.07	0.15	1.92	-	-	-	-	-	-	-	-	-	-	-	-
Anterior orbital gyrus R	55	0.01	0.06	0.15	2.18	-	-	-	-	-	-	-	-	0.22	3.34	-	-
Inferior frontal gyrus L	56	0.06	0.06	0.22	<b>2.87</b>	0.23	3.03	-	-	-	-	-	-	-	-	-	-
Inferior frontal gyrus R	57	0.09	0.07	-	-	0.27	2.70	-	-	-	-	-	-	-	-	-	-
Superior frontal gyrus L	58	0.04	0.05	0.20	<b>2.94</b>	0.15	2.11	-	-	-	-	0.17	2.46	-	-	-	-
Superior frontal gyrus R	59	0.04	0.07	-	-	0.23	2.95	-	-	-	-	-	-	-	-	-	-
Superior parietal gyrus L	62	0.01	0.06	-	-	0.15	2.48	-	-	-	-	-	-	-	-	-	-
Medial orbital gyrus L	68	0.08	0.07	0.30	<b>3.35</b>	-	-	-	-	-	-	-	-	-	-	-	-
Medial orbital gyrus R	69	0.08	0.08	0.24	2.11	0.26	2.25	-	-	-	-	-	-	-	-	-	-
Lateral orbital gyrus L	70	0.05	0.07	0.36	<b>4.50</b>	0.18	1.87	-	-	-	-	-	-	0.29	3.43	-	-
Lateral orbital gyrus R	71	0.04	0.07	0.19	1.99	-	-	-	-	-	-	-	-	0.34	3.97	-	-
Posterior orbital gyrus L	72	0.04	0.05	0.33	<b>5.26</b>	-	-	-	-	-	-	-	-	-	-	-	-
Posterior orbital gyrus R	73	0.07	0.08	0.30	<b>2.79</b>	-	-	-	-	-	-	-	-	-	-	-	-
Substantia nigra L	74	0.26	0.11	-	-	-	-	-	-	-	-	0.54	2.56	-	-	-	-
Substantia nigra R	75	0.22	0.13	0.49	2.13	-	-	-	-	-	-	-	-	-	-	-	-
Subgenual frontal cortex L	76	-0.01	0.08	0.24	<b>3.09</b>	-	-	-	-	-	-	-	-	-	-	-	-
Subgenual frontal cortex R	77	-0.05	0.05	0.12	<b>3.49</b>	0.06	2.30	-	-	-	-	-	-	-	-	-	-
Subcallosal area L	78	0.14	0.12	0.39	2.05	-	-	0.47	2.63	-	-	-	-	-	-	-	-
Subcallosal area R	79	0.11	0.08	0.31	2.35	0.34	2.79	-	-	-	-	-	-	-	-	-	-
Presubgenual frontal cortex L	80	0.11	0.09	0.32	2.29	-	-	-	-	-	-	-	-	-	-	-	-
Presubgenual frontal cortex R	81	0.02	0.07	0.19	2.24	0.25	3.10	-	-	-	-	-	-	-	-	-	-
Superior temporal gyrus anterior part L	82	0.08	0.08	0.38	<b>3.72</b>	-	-	-	-	-	-	0.39	<b>3.87</b>	-	-	-	-

Abbreviations: L=Left; R=Right

**Supplementary Figure 1. Axial slices of the [ $^{11}\text{C}$ ]PK11195 (left) and [ $^{18}\text{F}$ ]AV-1451 (right) binding potential ( $\text{BP}_{\text{ND}}$ ) maps for each patient (A-G). For comparison, the last row shows the corresponding average  $\text{BP}_{\text{ND}}$  maps across 15 controls. Patients A and B are MAPT mutation carriers; cases C and D are patients with GRN mutations; and patients E, F and G are C9orf72 mutation carriers. The  $\text{BP}_{\text{ND}}$  maps were spatially normalised to ICBM 152 2009a space, masked and smoothed (isotropic 6mm full width at half maximum Gaussian). The  $\text{BP}_{\text{ND}}$  maps are overlaid on the ICBM 152 2009a T1 MR template and the slices are reported in the neurological display convention (left on the left). The  $\text{BP}_{\text{ND}}$  scale applies to both radioligands.**

