

# Supplementary Material

## Assessment of Tau Pathology as Measured by <sup>18</sup>F-THK5317 and <sup>18</sup>F-Flortaucipir PET and Their Relation to Brain Atrophy and Cognition in Alzheimer's Disease

**Supplementary Table 1.** Characteristics of Karolinska Institutet cohort (KI) (restricted to the subset of  $n=4$  older healthy controls), and Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort.

	KI cohort				ADNI cohort				Comparison KI versus ADNI statistical test results		
	HC	pAD	AD	Statistical test results	HC	pAD	AD	Statistical test results	HC	pAD	AD
<i>n</i>	4	11	9		9	11	9				
Age, y mean (SD)	63 (6)	69 (7)	67 (7)	H = 2.64 p = 0.27	64 (2)	69 (5)	71 (7)	H = 8.58 p = 0.01 (HC < AD)	U = 13.50 p = 0.54	U = 60.50 p > 0.99	U = 27.50 p = 0.27
Sex m/f	3/1	5/6	2/7	$\chi^2 = 3.29$ p = 0.19	4/5	7/4	4/5	$\chi^2 = 1.01$ p = 0.60	$\chi^2 = 1.04$ p = 0.31	$\chi^2 = 0.73$ p = 0.39	$\chi^2 = 1.00$ p = 0.32
<i>APOE</i> $\epsilon 4$ positive/negative	NA	6/4	8/1	$\chi^2 = 2.04$ p = 0.15	NA	8/2	7/1	$\chi^2 = 0.18$ p = 0.67	NA	$\chi^2 = 0.95$ p = 0.33	$\chi^2 = 0.01$ p = 0.93
Education, y mean (SD)	15 (2)	12 (3)	13 (3)	H = 2.24 p = 0.33	16 (2)	15 (3)	16 (3)	H = 1.03 p = 0.60	U = 7 p = 0.22	U = 27 p = 0.02	U = 20 p = 0.07
Brain volume index mean (SD)	26.8 (13.5)	25.1 (8.6)	17.9 (8.2)	H = 4.50 p = 0.11	35.5 (9.9)	27.4 (12.3)	20.1 (8.0)	H = 7.98 p = 0.02 (AD < HC)	U = 11 p = 0.33	U = 57 p = 0.85	U = 32 p = 0.49
MMSE mean (SD)	NA	28 (3)	23 (3)	U = 10 p = 0.002	NA	28 (2)	22 (4)	U = 4.5 p < 0.001	NA	U = 55 p = 0.73	U = 34.50 p = 0.62
RAVL learning mean (SD)	NA	35 (10)	21 (6)	U = 7 p < 0.001	NA	39 (10)	20 (9)	U = 5 p < 0.001	NA	U = 44 p = 0.29	U = 33.50 p = 0.56

*APOE*  $\epsilon 4$  status was missing for one prodromal AD (pAD) patient in the KI cohort, and for one pAD and one AD dementia patient in the ADNI cohort. *APOE*  $\epsilon 4$  status was not available in the healthy control (HC) group in the KI cohort, and therefore these data were not collected for the HC group in the ADNI cohort.

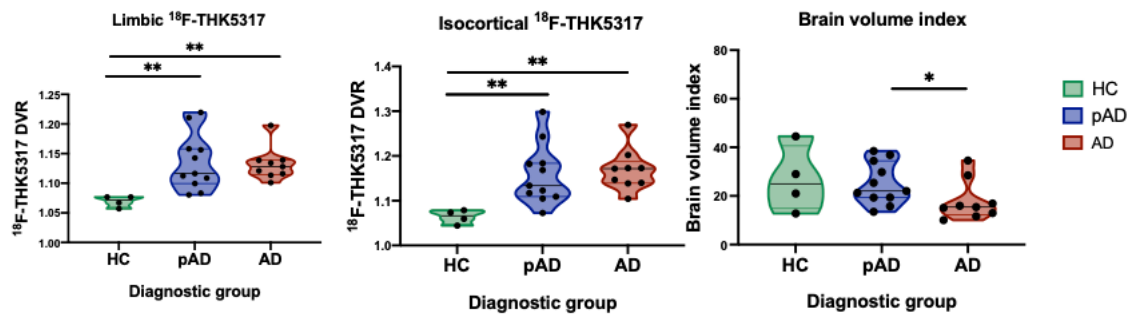
ADNI, Alzheimer's Disease Neuroimaging Initiative; *APOE*, apolipoprotein E; H, Kruskal-Wallis statistic; HC, healthy control; KI, Karolinska Institutet; MMSE, Mini-Mental State Examination; pAD, prodromal Alzheimer's disease; RAVL, Rey Auditory Verbal Learning; U, Mann-Whitney statistic

**Supplementary Table 2.** Discriminative ability of regional <sup>18</sup>F-THK5317 distribution volume ratio (DVR), <sup>18</sup>F-flortaucipir standardized uptake volume ratio (SUVr) and brain volume index across diagnostic groups in the KI cohort (restricted to the subset of *n*=4 older healthy controls) and the ADNI cohorts.

	AD dementia versus healthy controls		Prodromal AD versus healthy controls		AD dementia versus prodromal AD	
	KI (regional <sup>18</sup> F-THK5317 or brain volume index)	ADNI ( <sup>18</sup> F-flortaucipir or brain volume index)	KI (regional <sup>18</sup> F-THK5317 or brain volume index)	ADNI ( <sup>18</sup> F-flortaucipir or brain volume index)	KI (regional <sup>18</sup> F-THK5317 or brain volume index)	ADNI ( <sup>18</sup> F-flortaucipir or brain volume index)
	AUC (SE)	AUC (SE)	AUC (SE)	AUC (SE)	AUC (SE)	AUC (SE)
	p	p	p	p	p	p
Fusiform gyrus tau	0.94 (0.06) p = 0.01*	0.98 (0.03) p < 0.001***	0.95 (0.05) p = 0.009**	0.79 (0.11) p = 0.03*	0.58 (0.13) p = 0.57	0.85 (0.09) p = 0.009**
Parahippocampal gyrus tau	1.00 (0.00) p = 0.005**	0.98 (0.03) p < 0.001***	1.00 (0.00) p = 0.004**	0.84 (0.09) p = 0.01*	0.58 (0.13) p = 0.57	0.82 (0.10) p = 0.02*
Middle and inferior temporal gyrus tau	1.00 (0.00) p = 0.005**	1.0 (0.0) p < 0.001***	0.95 (0.06) p = 0.009**	0.81 (0.10) p = 0.02*	0.66 (0.13) p = 0.24	0.84 (0.09) p = 0.01*
Posterior cingulate cortex tau	0.89 (0.09) p = 0.03*	0.93 (0.07) p = 0.002**	0.89 (0.10) p = 0.03*	0.72 (0.12) p = 0.10	0.62 (0.13) p = 0.38	0.80 (0.11) p = 0.03*
Limbic composite tau	1.00 (0.00) p = 0.005**	0.98 (0.03) p < 0.001***	1.00 (0.00) p = 0.004**	0.82 (0.10) p = 0.02*	0.53 (0.13) p = 0.85	0.81 (0.11) p = 0.02*
Isocortical composite tau	1.00 (0.00) p = 0.005**	0.93 (0.07) p = 0.002**	0.95 (0.05) p = 0.009**	0.78 (0.11) p = 0.04*	0.60 (0.13) p = 0.47	0.80 (0.11) p = 0.03*
Brain volume index	0.72 (0.17) p = 0.22	0.86 (0.09) p = 0.009**	0.50 (0.20) p > 0.99	0.73 (0.12) p = 0.09	0.78 (0.11) p = 0.04*	0.71 (0.12) p = 0.12

AD, Alzheimer's disease; ADNI, Alzheimer's Disease Neuroimaging Initiative; AUC, area under the curve; DVR, distribution volume ratio; SE, standard error

\*p<0.05; \*\*p < 0.01; \*\*\*p < 0.001



**Supplementary Figure 1.** Violin plots illustrating patterns of tau PET uptake as measured by  $^{18}\text{F-THK5317}$  in the limbic and isocortical composite regions, as well as brain volume index across healthy controls (HCs), prodromal AD (pAD), and AD dementia groups in the KI cohort (restricted to the subset of  $n=4$  older HCs).