Additional File 1

Table S1 Effect of *TREM2* p.R47H status and influenza vaccine on TSPO binding

	MCI (*n* = 6)	***TREM2* p.R47H (*n* = 5)**
Age (years) (Median + IQR)	70.7 (66.0 - 77.3)	61.7 (59.5 - 67.0)[a]
Sex (Male/Female)	6 / 0	2 / 3
TSPO genotype (MAB/HAB)	4 / 2	4 / 1
APOEε4 (carrier/non-carrier)	4 / 2	3 / 2
WM - Hypointensity volume (cm^3) (Median + IQR)	2.8 (1.4 - 7.2)	1.6 (1.2 – 5.5)

HAB = high-affinity binder; IQR = interquartile range; MAB = mixed-affinity binder; MCI = mild cognitive impairment; TSPO = translocator protein; WM = white matter.

APOEε4 carrier refers to the number with ≥1 ε4 allele.

[a]*TREM2* p.R47H carrier significant versus MCI group; $P < 0.05$.

Table S2 Baseline comparison of regional TSPO binding

	Imaging Controls (*n* = 8)	**MCI (*n* = 8)**	***TREM2* p.R47H (*n* = 8)**
Braak I (mean ± SD)	1.13 ± 0.03	1.12 ± 0.05	1.12 ± 0.03
Braak II (mean ± SD)	1.20 ± 0.06	1.23 ± 0.05	1.18 ± 0.05[a]
Braak III (mean ± SD)	1.09 ± 0.03	1.11 ± 0.04	1.09 ± 0.02[a]
Braak IV (mean ± SD)	1.05 ± 0.01	1.08 ± 0.04	1.08 ± 0.02
Braak V (mean ± SD)	1.00 ± 0.02	1.02 ± 0.03	1.04 ± 0.04
Braak VI (mean ± SD)	1.02 ± 0.03	1.00 ± 0.05	1.03 ± 0.04

General linear model results for TSPO DVR values based on Braak regions. *TREM2* p.R47H group separately compared to the MCI and imaging control groups. Age and TSPO status as covariates for statistical comparison.

[a]*TREM2* p.R47H carrier significant *versus* MCI group; $P < 0.05$.

DVR = distribution volume ratio; MCI = mild cognitive impairment; SD = standard deviation; TSPO = translocator protein.

Table S3 Effect of *TREM2* p.R47H status and influenza vaccine on TSPO binding

	Beta	CI Lower	CI higher	SE	df	t	sig
Braak I							
Vaccine response	0.016	-0.025	0.058	0.018	9.0	0.892	0.40
Group*vaccine response	-0.030	-0.091	0.032	0.027	9.0	-1.098	0.30
Braak II							
Vaccine response	0.005	-0.022	0.031	0.01	5.4	0.448	0.67
Group*vaccine response	-0.034	-0.073	0.005	0.015	5.4	-2.195	0.08
Braak III							
Vaccine response	-0.001	-0.018	0.016	0.008	12.6	-0.123	0.90
Group*vaccine response	-0.022	-0.046	0.003	0.011	12.6	-1.904	0.08
Braak IV							
Vaccine response	0.001	-0.012	0.014	0.006	10.0	0.13	0.90
Group*vaccine response	-0.019	-0.038	0.000	0.009	10.0	-2.171	0.06
Braak V							
Vaccine response	0.003	-0.014	0.021	0.008	9.3	0.425	0.68
Group*vaccine response	-0.010	-0.036	0.016	0.012	9.3	-0.878	0.40
Braak VI							
Vaccine response	0.003	-0.016	0.022	0.008	9.448	0.382	0.71
Group*vaccine response	-0.007	-0.036	0.021	0.013	9.448	-0.574	0.58

Linear mixed models results for change in TSPO DVR in Braak regions, in response to influenza vaccine challenge and comparison of vaccine response between the *TREM2* p.R47H carrier group relative to the mild cognitive impairment group (Group*vaccine response). Age and TSPO binding status were included as covariates.

CI = confidence interval; df = degrees of freedom; SE = Standard error.

Table S4 Comparison of regional tau binding

	MCI (*n* = 8)	***TREM2* p.R47H (*n* = 8)**
Braak I (mean ± SD)	1.18 ± 0.19	1.14 ± 0.12
Braak II (mean ± SD)	1.24 ± 0.17	1.25 ± 0.06
Braak III (mean ± SD)	1.12 ± 0.09	1.14 ± 0.05
Braak IV (mean ± SD)	1.11 ± 0.08	1.12 ± 0.05
Braak V (mean ± SD)	1.02 ± 0.07	1.06 ± 0.03
Braak VI (mean ± SD)	0.95 ± 0.06	1.01 ± 0.04[a]

General linear model results for tau SUVR values across Braak regions. Comparison made between mild cognitive impairment (MCI) and *TREM2* p.R47H carrier groups. Age was used as a covariate.

MCI = mild cognitive impairment; SD = standard deviation; SUVR = standardised uptake value.

[a]*TREM2* p.R47H carrier significant *versus* MCI group; $P < 0.05$.

Table S5 Clinical assessment scores and cognitive battery results

Clinical assessments	**Clinical Controls**		**MCI**		***TREM2* p.R47H**	
GDS (median + IQR)	*n* = 29	2.0 (1.0-5.0)	*n* = 11	10.0 (6.0-12.0)	*n* = 12	1.5 (0.0-5.5)[b]
HAM-A (median + IQR)	*n* = 28	3.0 (1.0-6.0)	*n* = 11	7.0 (2.0-12.0)	*n* = 12	1.5 (1.0-5.0)[b]
QoL-AD (mean ± SD)	*n* = 29	42.0 ± 5.0	*n* = 11	35.2 ± 4.5	*n* = 12	41.2 ± 6.7[b]
FSS (median + IQR)	*n* = 27	21.0 (15.0-31.0)	*n* = 11	34.0 (24.0-39.0)	*n* = 11	18.0 (9.0-30.0)[b]
AES (mean ± SD)	*n* = 29	63.8 ± 5.5	*n* = 11	66.1 ± 3.4	*n* = 12	66.2 ± 3.4[b]
Cognitive battery						
FAS (mean ± SD)	*n* = 29	47.9 ± 12.7	*n* = 11	44.1 ± 14.6	*n* = 11	48.5 ± 16.7
Animal naming (mean ± SD)	*n* = 29	23.0 ± 5.5	*n* = 11	19.7 ± 3.9	*n* = 11	23.3 ± 7.4
TMT-A (median + IQR)	*n* = 29	33.5 (26.9-37.2)	*n* = 11	35.8 (30.3-51.6)	*n* = 11	37.2 (27.0-41.8)
TMT-B (median + IQR)	*n* = 29	61.2 (51.4-75.6)	*n* = 11	86.6 (62.8-116.6)	*n* = 11	61.9 (49.6-82.5)
ADAS-Cog 13 (median + IQR)	*n* = 29	5.3 (3.0-8.0)	*n* = 11	12.0 (10.3-16.3)	*n* = 11	6.7 (4.0-8.3)[a]
DMS (mean ± SD)	*n* = 28	88.9 ±6.1	*n* = 11	87.0 ± 7.7	*n* = 11	86.1 ± 6.[a]
OTS 1st choice (mean ± SD)	*n* = 25	17.2 ± 4.4	*n* = 10	13.1 ± 3.8	*n* = 11	17.0 ± 2.3
OTS MCC (median + IQR)	*n* = 25	1.3 (1.2-1.6)	*n* = 11	1.6 (1.4-2.0)	*n* = 11	1.4 (1.3-1.5)
OTS MLC (median + IQR)	*n* = 25	28.2 (20.2-52.5)	*n* = 11	47.0 (40.0-82.0)	*n* = 11	23.4 (15.6-35.3)
PAL TE (median + IQR)	*n* = 28	9.5 (6.3-24.0)	*n* = 11	21.0 (13.0-40.0)	*n* = 11	13.0 (8.0-17.0)
PAL TE 6 shapes (median + IQR)	*n* = 28	2.5 (0.0-6.0)	*n* = 11	10.0 (3.0-17.0)	n=11	4.0 (2.0-5.0)
PRM (median + IQR)	*n* = 28	87.5 (83.3-95.8)	*n* = 11	83.3 (79.2-87.5)	*n* = 11	91.7 (83.3-95.8)
RTI simple reaction (mean ± SD)	*n* = 27	322.7 ± 44.6	*n* = 11	370.5 ± 74.4	*n* = 10	328.4 ± 68.3
RTI five choice (median + IQR)	*n* = 27	357.0 (307.0-398.0)	*n* = 11	338.5 (328.0-409.5)	*n* = 10	350.0 (298.6-437.6)
RVP mean latency (median + IQR)	*n* = 26	457.9 (403.3-592.4)	*n* = 9	459.8 (407.2-540.1)	*n* = 10	459.7 (427.9-493.2)
SSP span length (mean ± SD)	*n* = 25	5.6 ± 1.7	*n* = 10	5.0 ± 1.1	*n* = 11	6.0 ± 1.3
SWM between errors (mean ± SD)	*n* = 28	37.5 ± 29.2	*n* = 11	47.5 ± 16.9	*n* = 11	36.0 ± 17.1
SWM strategy (mean ± SD)	*n* = 28	32.2 ± 8.1	*n* = 11	37.3 ± 5.2	*n* = 11	36.4 ± 4.8

General linear model results for clinical and cognitive assessments values. *TREM2* p.R47H group separately compared to the MCI and clinical control groups. For the cognitive battery age and education were used as covariates. Untransformed values presented.

[a]*TREM2* p.R47H carrier significant *versus* controls; $P < 0.05$.

[b]*TREM2* p.R47H carrier significant *versus* MCI group; $P < 0.05$.

AES = apathy evaluation score; DMS = delayed matching to sample; FFS = fatigue severity scale; GDS = geriatric depression scale; HAM-A = Hamilton Anxiety Rating Scale; IQR = interquartile range; MCC = mean choices to correct; MCI = mild cognitive impairment; MLC = mean latency to correct; OTS = one touch stockings of Cambridge; PAL = paired associates learning; PRM = Pattern Recognition memory; QoL-AD = Quality of life in Alzheimer's disease; RTI = reaction time; RVP = rapid visual information processing; SD = standard deviation; SSP = spatial span; SWM = spatial working memory; TE = total errors; TMT = trail-making task.

Figure S1: Amyloid status and early tau burden. Pooled analysis showing tau Braak I region SUVR values based on amyloid status. High Braak I tau burden is noticeable in amyloid positive participants. SUVR = standardised uptake value ratio.