1. Supplemental Methods

Measures

The following measures were used to examine the psychopathology in the first episode psychosis: Positive and Negative Syndrome Scale, PANSS(1); Scale for the Assessment of Negative Symptoms, SANS(2); Calgary Depression Scale, depression scale(3); Snaith-Hamilton Pleasure Scale, pleasure scale(4); Apathy Evaluation Scale, apathy scale(5); Global Assessment of Functioning, GAF(6).

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), was used to assess cognitive function in first episode psychosis. It has been validated in psychotic patients and comprises five subscales: immediate memory, visuospatial ability, language, attention, and delayed memory (7, 8).

MRI data acquisition

Proton density-weighted (PD) brain MRI scans (TE = 17, TR = 6000, FOV = 22 cm, matrix = 256 × 256, slice thickness = 2 mm, number of excitations = 2) was obtained for each subject using a 1.5T Signa scanner (General Electric Medical Systems, Milwaukee, WI, USA) for 6 of healthy volunteers and 11 of first episode psychosis. For the remaining 8 patients with first episode psychosis and 14 healthy volunteers, PD MRI images (TE= Min full, TR = 6000, FOV = 22 cm, slice thickness = 2 mm, and number of acquisitions = 1) were acquired using a 3T MR-750 scanner (General Electric Medical Systems). MRI images were used for the anatomical delineation of regions and the quantification of PET images. As we previously reported (9, 10), differences in MRI acquisition parameters and scanner used did not have a significant effect on [^{18}F]FEPPA outcome measures (data not shown).

PET data acquisition

All [^{18}F]FEPPA PET scans were performed using a high-resolution CPS- high resolution research tomograph PET scanner (Siemens Molecular Imaging, Knoxville, TN, USA), which measures radioactivity in 207 1.2-mm thick slices. Dynamic emission data were acquired for 125 minutes (34 time frames: 1 frame of variable length, 5 × 30 s, 1 × 45 s, 2 × 60 s, 1 × 90 s, 1 × 120 s, 1 × 210 s, and 22 × 300 s) following an intravenous bolus injection of 182.94 ± 13.08 (mean ± SD) MBq of [^{18}F]FEPPA.

Kinetic parameters of [^{18}F]FEPPA were derived from the time activity curves using two-tissue compartment model and plasma input function to obtain the binding outcome measure total distribution volume (V_T) for each region of interest, which has been validated for [^{18}F]FEPPA quantification (11). Kinetic analysis of regions of interest incorporated a 5% contribution from the blood in the vascular lumen (12) in the fitting of the two-compartment kinetic model using PMOD software (PMOD Technologies, Zurich, Switzerland).

Voxel-based PET image analysis

Parametric images of [^{18}F]FEPPA V_T were generated using the Logan graphical analysis method (14), A wavelet-based kinetic modeling approach was applied to increase the signal-to-noise ratio while maintaining the resolution (15). To examine voxel-wise group differences of V_T, an independent sample T-test was conducted using Statistical Parametric Mapping (SPM8- http://www.fil.ion.ucl.ac.uk/spm/software/spm8). TSPO genotype (rs6971 polymorphism) was included as a covariate. Significant level for the whole brain analysis was thresholded at $p<0.05$, FWE corrected at the voxel level.

Input function measurement

Arterial blood was collected for the first 22.5 min after radiotracer injection at a rate of 2.5 mL/min and blood radioactivity levels were measured using an automatic blood sampling system (Model PBS-101, Veenstra Instruments, Joure, Netherlands). Additionally, 7 mL blood samples were drawn manually at -5, 2.5, 7, 12, 15, 20, 30, 45, 60, 90, and 120 min following tracer injection. The relative proportion of radiolabeled metabolites was measured using high-

performance liquid chromatography (HPLC) and dispersion- and metabolite-corrected plasma input function was generated as previously described (16, 17).

TSPO polymorphism genotyping

Using high salt extraction method, DNA samples were extracted from peripheral white blood cells (18). A single-nucleotide polymorphism (rs6971), which is known to affect binding of second-generation TSPO PET radioligands (17, 19-21), was genotyped using a TaqMan assay (Applied Biosystems, Foster City, CA, USA), as previously described (9, 10).

2. Supplemental Results

Differences in [^{18}F]FEPPA V_T between psychotic patients and healthy volunteers

After excluding subjects who were not in their first episode of psychosis (n=4), the group effects on V_T remained non-significant ($F_{(2, 31)}$ = 1.04, P = .37) and healthy volunteers had non-significant higher uptake (15.4%) than first episode psychosis in hippocampus ($F_{(1, 32)}$ = 1.87, p = .18) and dorsolateral prefrontal cortex ($F_{(1, 32)}$ = 0.42, p = .52, 6.1% higher in healthy volunteers than first episode psychosis). Same results remain after correction for partial volume effects ($F_{(2,31)}$ =.96, p = .39), the non-significant elevated uptake of healthy volunteers remained in hippocampus ($F_{(1, 32)}$ = 1.77, p = .19, 14.7% higher in healthy volunteers than first episode psychosis) and dorsolateral prefrontal cortex ($F_{(1, 32)}$ = 0.49, p = .49, 6.6% higher in healthy volunteers than first episode psychosis).

Differences in DVR with cerebellum as denominator (DVR $_{cer}$) between first episode psychosis and healthy volunteers

There was no significant group effect on [^{18}F]FEPPA V_T in cerebellum, before ($F_{(1,36)}$ = .07, p = .80) or after correction for partial volume effects ($F_{(1,36)}$ = .08, p = .77).

We found no significant effect of clinical group on DVR $_{cer}$ ($F_{(2, 35)}$ = 1.87, p = .17). While not statistically significant, healthy volunteers show higher DVR in hippocampus ($F_{(1,36)}$ = 2.42, p = .13; 12.1% higher in healthy volunteers than first episode psychosis) and dorsolateral prefrontal cortex ($F_{(1,36)}$ = 2.64, p = .11; 6.7% higher in healthy volunteers than first episode psychosis).

Information on the results after partial volume correction and also other regions of interest is reported in ST2.

Differences in DVR with whole brain as denominator (DVR $_{WB}$) between first episode psychosis and healthy volunteers

[^{18}F]FEPPA V_T of whole brain did not differ significantly between the two clinical groups before ($F_{(1,36)}$ = .13, p = .73) or after partial volume effect correction ($F_{(1,36)}$ = .48, p = .49).

No significant differences in DVR $_{WB}$ were observed between the groups ($F_{(2, 35)}$ = 1.66, p = .21). Although not significant, healthy volunteers had higher DVR $_{WB}$ than first episode psychosis in hippocampus ($F_{(1, 36)}$ = 1.71, p = .20; 9.4% higher in healthy volunteers than first episode psychosis) and dorsolateral prefrontal cortex ($F_{(1, 36)}$ = 1.71, p = .20; 3.7% higher in healthy volunteers than first episode psychosis). Results of analysis after partial volume correction and other regions of interest are reported in ST3.

Differences in DVR gray matter as denominator (DVR_{GM}) between first episode psychosis and healthy volunteers

We found no significant difference between [^{18}F]FEPPA V_T in gray matter between first episode psychosis and healthy volunteers before ($F_{(1,36)}$ = .202, p = .656) and after correction for partial volume effects ($F_{(1,36)}$ = .68, p = .42).

No significant difference was observed between groups in DVR_{GM} ($F_{(2,35)}$ = 1.12, p = .34). Although not significant, healthy volunteers showed higher DVR_{GM} than first episode psychosis in dorsolateral prefrontal cortex ($F_{(1, 36)}$ = 1.30, p = .26; 2.9% higher in healthy volunteers than first episode psychosis) and hippocampus ($F_{(1, 36)}$ = 1.10, p = .30; 8% higher in healthy volunteers than first episode psychosis). Results of analysis after partial volume correction and other regions of interest are reported in ST4.

Correlation between [^{18}F]FEPPA V_T and length of illness, severity of symptoms, clinical and neuropsychological measures

We observed a correlation between with RBANS total score and [^{18}F]FEPPA V_T in hippocampus with the partial volume corrected data ($r = .51$, $p = .04$)

In exploratory correlation analysis after removing 4 participants whom duration of illness is longer than 5 years, we found significant negative correlation between PANSS general subscore and [^{18}F]FEPPA V_T in GM before ($r = -.57$, $p = .03$) and after correction for partial volume effects ($r = -.56$, $p = .04$). Moreover we found a significant association of [^{18}F]FEPPA V_T in WB after partial volume effect correction and PANSS general subscore ($r = -.54$, $p = .05$).

2. Supplemental Tables

TABLE S1. Regional [^{18}F]FEPPA V_T between first episode psychosis and healthy volunteers. Factorial ANOVA were performed for each region of interest to examine the diagnostic groups effect with genotype added as covariates. % difference was calculated as the difference in [^{18}F]FEPPA V_T between the groups (V_T first episode psychosis – V_T healthy volunteers) divided by [^{18}F]FEPPA V_T of the healthy volunteers group times 100.

		HV (n = 20)		FEP (n = 19)		Percent Difference	Diagnostic effect		Effect size
	ROI	Adjusted mean	SE	Adjusted mean	SE	%	$F_{(1, 36)}$	P	η^2
V_T	DLPFC	10.26	0.62	9.64	0.64	-6.07	0.49	0.49	.01
	HC	10.47	0.74	9.07	0.76	-13.38	1.74	0.20	.05
	MPFC	9.41	0.58	9.14	0.59	-2.84	0.11	0.75	.00
	Temporal cortex	10.35	0.60	10.00	0.62	-3.35	0.16	0.69	.01
	GM	9.69	0.58	9.32	0.59	-3.83	0.20	0.66	.01
	WB	8.96	0.53	8.69	0.54	-3.00	0.13	0.73	.00
	Cerebellum	10.34	0.74	10.61	0.76	2.61	0.07	0.80	.00
PVEC V_T	DLPFC	12.71	0.77	11.81	0.79	-7.06	0.67	0.42	.02
	HC	10.98	0.77	9.50	0.79	-13.48	1.82	0.19	.05
	MPFC	10.35	0.63	10.15	0.65	-1.96	0.05	0.82	.00
	Temporal cortex	11.67	0.69	11.41	0.70	-2.19	0.07	0.80	.00
	GM	12.06	0.75	11.18	0.76	-7.29	0.68	0.42	.02
	WB	12.34	0.77	11.57	0.79	-6.23	0.48	0.49	.01
	Cerebellum	11.06	0.76	11.38	0.77	2.82	0.08	0.77	.00

Abbreviations: DLPFC, dorsolateral prefrontal cortex; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; HV, healthy volunteer; MPFC, medial prefrontal cortex; ; SE, standard error; V_T, Volume of distribution; WB, whole brain.

TABLE S2. Regional distribution volume ratio of cerebellum (DVR_{Cer}) between first episode psychosis and healthy volunteers. DVR_{Cer} was calculated as the ratio [^{18}F]FEPPA V_T of region to [^{18}F]FEPPA V_T of cerebellum. % difference was calculated as the difference in DVR_{Cer} between the groups (V_T first episode psychosis – V_T healthy volunteers) divided by DVR_{Cer} of the healthy volunteers group times a 100.

		HV (n = 20)		FEP (n = 19)		Percent Difference	Diagnostic effect		Effect size
	ROI	**Adjusted mean**	**SE**	**Adjusted mean**	**SE**	**%**	**F (1, 36)**	**P**	**η^2**
DVR_{Cer}	**DLPFC**	1.00	0.03	0.94	0.03	-6.77	2.64	0.11	.07
	HC	1.02	0.06	0.89	0.06	-12.09	2.42	0.13	.06
	MPFC	0.92	0.03	0.89	0.03	-3.47	0.65	0.43	.02
	Temporal cortex	1.01	0.03	0.98	0.03	-2.48	0.33	0.57	.01
	GM	0.95	0.03	0.90	0.03	-4.64	1.55	0.22	.04
	WB	0.88	0.02	0.84	0.02	-3.99	1.29	0.26	.04
DVR_{Cer} with PVEC	**DLPFC**	1.17	0.04	1.06	0.04	-8.83	4.10	0.05	.10
	HC	1.00	0.05	0.87	0.05	-13.20	3.08	0.09	.08
	MPFC	0.95	0.03	0.92	0.03	-3.78	0.70	0.41	.02
	Temporal cortex	1.06	0.03	1.04	0.03	-2.53	0.32	0.57	.01
	GM	1.10	0.03	1.00	0.03	-9.07	5.84	0.02	.14
	WB	1.13	0.03	1.04	0.03	-8.07	4.70	0.04	.12

Abbreviations: DLPFC, dorsolateral prefrontal cortex; DVR, distribution volume ratio; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; ; HV, healthy volunteer; MPFC, medial prefrontal cortex; ; ROI, region of interest; SE, standard error; WB, whole brain.

TABLE S3. Regional distribution volume ratio of whole brain (DVR_{WB}) between first episode psychosis and healthy volunteers. DVR_{WB} was calculated as the ratio [^{18}F] FEPPA V_T of region to [^{18}F] FEPPA V_T of whole brain. % difference was calculated as the difference in DVR_{WB} between the groups (V_T first episode psychosis – V_T healthy volunteers) divided by DVR_{WB} of the healthy volunteers group times a 100.

		HV (n = 20)		FEP (n = 19)		Percent Difference	Diagnostic effect		Effect Size
	ROI	Adjusted mean	SE	Adjusted mean	SE	%	$F_{(1, 36)}$	P	η^2
DVR_{WB}	DLPFC	1.15	0.02	1.11	0.02	-3.74	1.71	0.20	.05
	HC	1.17	0.05	1.06	0.06	-9.43	1.71	0.20	.05
	MPFC	1.05	0.02	1.05	0.02	-0.18	0.01	0.94	.00
	Temporal cortex	1.15	0.02	1.17	0.03	1.04	0.08	0.78	.00
	GM	1.08	0.00	1.07	0.01	-1.01	0.99	0.33	.03
	Cerebellum	1.15	0.04	1.23	0.05	7.07	1.37	0.25	.04
DVR_{WB} with PVEC	DLPFC	1.04	0.01	1.02	0.02	-1.25	0.28	0.60	.01
	HC	0.89	0.05	0.85	0.05	-4.06	0.26	0.62	.01
	MPFC	0.85	0.01	0.88	0.02	-0.18	3.52	0.07	.09
	Temporal cortex	0.94	0.03	1.01	0.04	1.04	1.94	0.17	.05
	GM	0.98	0.00	0.97	0.00	-1.01	4.23	0.05	.11
	Cerebellum	0.89	0.04	1.01	0.05	7.07	3.12	0.07	.08

Abbreviations: DLPFC, dorsolateral prefrontal cortex; DVR, distribution volume ratio; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; HV, healthy volunteer; MPFC, medial prefrontal cortex; ; ROI, region of interest; SE, standard error; WB, whole brain.

TABLE S4. Regional distribution volume ratio of gray matter (DVR_{GM}) between first episode psychosis and healthy volunteers. DVR_{GM} was calculated as the ratio [^{18}F] FEPPA V_T of region to [^{18}F] FEPPA V_T of gray matter. % Difference was calculated as the difference in DVR_{GM} between the groups (V_T first episode psychosis – V_T healthy volunteers) divided by DVR_{GM} of the healthy volunteers group times a 100.

		HV (n = 20)		FEP (n = 19)		Percent Difference	Diagnostic effect		Effect size
	Gray matter ROI	Adjusted mean	SE	Adjusted mean	SE	%	$F_{(1, 36)}$	P	η^2
DVR_{GM}	DLPFC	1.06	0.02	1.03	0.02	-2.91	1.30	0.26	.04
	HC	1.08	0.06	0.99	0.06	-7.97	1.10	0.30	.03
	MPFC	0.98	0.02	0.98	0.02	0.61	0.07	0.80	.00
	Temporal cortex	1.07	0.03	1.09	0.03	2.34	0.34	0.56	.01
	Cerebellum	1.06	0.05	1.15	0.06	8.86	1.49	0.23	.04
	WB	0.93	0.00	0.94	0.01	1.07	1.06	0.31	.03
DVR_{GM} with PVEC	DLPFC	1.06	0.02	1.06	0.02	-0.09	0.00	0.97	.00
	HC	0.91	0.05	0.88	0.05	-3.08	0.14	0.72	.00
	MPFC	0.86	0.02	0.92	0.02	5.90	5.08	0.03	.12
	Temporal cortex	0.97	0.04	1.05	0.04	8.59	2.55	0.12	.07
	Cerebellum	0.91	0.05	1.04	0.05	14.48	3.68	0.06	.09
	WB	1.02	0.00	1.04	0.00	1.17	4.17	0.05	.10

Abbreviations: DLPFC, dorsolateral prefrontal cortex; DVR, distribution volume ratio; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; HV, healthy volunteer; MPFC, medial prefrontal cortex ; ROI, region of interest; SE, standard error; WB, whole brain.

TABLE S5. Association between regional [^{18}F] FEPPA V_T and psychopathology, adjusted for TSPO genotype (rs6971).

V_T	Age at onset		Number of crises		Length of illness		GAF	
	r	p	r	p	r	p	r	p
DLPFC	-0.09	0.78	-0.04	0.91	-0.56	0.06	-0.13	0.70
HC	-0.49	0.10	-0.21	0.51	-0.15	0.64	-0.16	0.61
MPFC	-0.25	0.43	-0.03	0.92	-0.49	0.10	-0.17	0.60
Temporal cortex	-0.31	0.32	-0.02	0.96	-0.47	0.12	-0.15	0.64
GM	-0.15	0.62	-0.09	0.79	-0.54	0.07	-0.18	0.57
WB	-0.14	0.67	-0.02	0.94	-0.49	0.10	-0.23	0.47
V_T with PVEC	r	p	r	p	r	p	r	p
DLPFC	-0.07	0.83	0.02	0.96	-0.56	0.06	-0.13	0.70
HC	-0.47	0.13	-0.27	0.40	-0.19	0.56	-0.16	0.62
MPFC	-0.17	0.59	-0.01	0.99	-0.48	0.11	-0.23	0.47
Temporal cortex	-0.25	0.43	-0.03	0.92	-0.48	0.11	-0.19	0.56
GM	-0.15	0.64	-0.13	0.70	-0.58	0.05	-0.16	0.62
WB	-0.14	0.67	-0.10	0.75	-0.55	0.06	-0.20	0.53

Abbreviations: DLPFC, dorsolateral prefrontal cortex; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; MPFC, medial prefrontal cortex; ; ROI, region of interest; SE, standard error; WB, whole brain.

TABLE S6. Association between [^{18}F]FEPPA V_T and PANSS scores in first episode psychosis, adjusted for TSPO genotype (rs6971).

V_T	Positive		Negative		General		Total	
ROI	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
DLPFC	-0.20	0.44	0.08	0.76	-0.28	0.25	-0.18	0.48
HC	-0.23	0.35	-0.11	0.67	-0.28	0.27	-0.27	0.28
MPFC	-0.16	0.52	-0.01	0.97	-0.28	0.26	-0.21	0.41
Temporal cortex	-0.25	0.32	0.02	0.95	-0.25	0.31	-0.21	0.42
GM	-0.28	0.26	0.02	0.95	-0.39	0.11	-0.29	0.25
WB	-0.33	0.18	0.05	0.85	-0.40	0.10	-0.30	0.23
V_T with PVEC	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
DLPFC	-0.14	0.59	0.03	0.90	-0.30	0.23	-0.19	0.45
HC	-0.19	0.46	-0.12	0.63	-0.28	0.27	-0.26	0.29
MPFC	-0.11	0.66	-0.03	0.92	-0.24	0.35	-0.18	0.48
Temporal cortex	-0.18	0.49	0.02	0.95	-0.22	0.38	-0.17	0.51
GM	-0.23	0.36	-0.02	0.94	-0.39	0.12	-0.29	0.25
WB	-0.22	0.38	0.01	0.96	-0.37	0.14	-0.26	0.30

Abbreviations: DLPFC, dorsolateral prefrontal cortex; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; MPFC, medial prefrontal cortex; ; ROI, region of interest; SE, standard error; WB, whole brain.

TABLE S7. Association between [^{18}F]FEPPA V_T and SANS scores in first episode psychosis, adjusted for TSPO genotype (rs6971). None of the significant correlations survived correction for multiple comparisons.

V_T	Affective		Inappropriate affect		Alogia		Avolition		Anhedonia		Attention		Total		Total global	
	R	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
DLPFC	0.18	0.47	-0.16	0.53	-0.06	0.82	-0.23	0.37	0.14	0.58	-0.12	0.64	0.01	0.96	-0.01	0.98
HC	0.08	0.74	-0.28	0.25	-0.39	0.11	-0.20	0.42	-0.17	0.50	**-0.48**	**0.04***	-0.28	0.41	-0.22	0.38
MPFC	0.13	0.62	-0.24	0.34	-0.22	0.37	-0.27	0.27	0.11	0.68	-0.18	0.47	-0.08	0.77	-0.08	0.76
Temporal cortex	0.13	0.62	-0.14	0.57	-0.16	0.54	-0.29	0.24	-0.01	0.96	-0.30	0.23	-0.09	0.72	-0.12	0.64
GM	0.21	0.40	-0.30	0.23	-0.18	0.48	-0.24	0.33	0.10	0.70	-0.15	0.56	-0.02	0.92	-0.04	0.88
WB	0.27	0.28	-0.30	0.23	-0.16	0.54	-0.19	0.46	0.11	0.68	-0.15	0.56	0.017	0.95	-0.00	0.99
V_T with PVEC	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
DLPFC	0.13	0.62	-0.02	0.48	-0.08	0.75	-0.23	0.37	0.14	0.59	-0.15	0.54	-0.02	0.94	-0.04	0.89
HC	0.05	0.85	-0.29	0.25	-0.41	0.10	-0.24	0.36	-0.18	0.47	**-0.48**	**0.04***	-0.23	0.35	-0.25	0.32
MPFC	0.10	0.69	-0.22	0.37	-0.21	0.41	-0.24	0.33	0.13	0.62	-0.16	0.52	-0.07	0.79	-0.05	0.84
Temporal cortex	0.10	0.69	-0.13	0.61	-0.14	0.57	-0.29	0.24	0.00	0.99	-0.29	0.24	-0.09	0.72	-0.11	0.66
GM	0.15	0.55	-0.31	0.21	-0.21	0.39	-0.28	0.27	0.09	0.72	-0.15	0.55	-0.07	0.78	-0.07	0.77
WB	0.18	0.47	-0.28	0.26	-0.20	0.44	-0.26	0.30	0.12	0.65	-0.15	0.56	-0.04	0.87	-0.05	0.83

** $p<0.05$; adjusted p-value threshold: $p<0.008$ for SANS subscales*

Abbreviations: DLPFC, dorsolateral prefrontal cortex; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; MPFC, medial prefrontal cortex; ; ROI, region of interest; SE, standard error; WB, whole brain.

TABLE S8. Association between [^{18}F]FEPPA V_T and RBANS scores in first episode psychosis (n = 18[#]), adjusted for TSPO genotype (rs6971).

V_T	Immediate memory		Visuospatial		Language		Attention		Delayed memory		Total	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
DLPFC	-0.11	0.69	-0.25	0.34	-0.22	0.41	-0.06	0.82	-0.08	0.78	-0.14	0.60
HC	0.40	0.12	0.35	0.17	0.28	0.28	**0.49**	**0.05***	0.27	0.30	**0.50**	**0.04***
MPFC	0.16	0.53	-0.00	0.99	-0.06	0.85	0.02	0.95	-0.03	0.91	0.07	0.78
Temporal cortex	0.18	0.50	0.16	0.55	-0.10	0.70	0.03	0.90	0.04	0.89	0.11	0.67
GM	0.03	0.92	-0.16	0.53	-0.21	0.43	-0.04	0.87	0.02	0.96	-0.05	0.85
WB	0.03	0.90	-0.17	0.51	-0.20	0.44	-0.05	0.85	0.02	0.94	-0.05	0.85
V_T with PVEC	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
DLPFC	-0.06	0.83	-0.17	0.51	-0.17	0.53	-0.07	0.80	-0.06	0.83	-0.08	0.75
HC	0.39	0.12	0.38	0.13	0.26	0.32	**0.49**	**0.05***	0.30	0.24	**0.51**	**0.04***
MPFC	0.20	0.45	0.05	0.84	-0.02	0.93	0.00	0.99	-0.02	0.93	0.10	0.70
Temporal cortex	0.19	0.46	0.21	0.43	-0.10	0.70	0.04	0.87	0.07	0.80	0.14	0.59
GM	0.07	0.79	-0.13	0.62	-0.15	0.57	-0.03	0.91	0.03	0.92	-0.01	0.98
WB	0.07	0.79	-0.14	0.59	-0.13	0.63	-0.02	0.94	0.02	0.94	-0.00	0.99

[#]Data was not available for one subject.

* *$p<0.05$; adjusted p-value threshold: $p<0.017$ for RBANS subscales*

Abbreviations: DLPFC, dorsolateral prefrontal cortex; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; MPFC, medial prefrontal cortex; ; ROI, region of interest; SE, standard error; WB, whole brain.

TABLE S9. Association between [^{18}F]FEPPA V_T and apathy scale, depression scale, and pleasure scale scores in first episode psychosis, adjusted for TSPO genotype (rs6971).

V_T	Apathy scale		Depression scale*		Pleasure Scale	
	r	p	r	p	r	p
DLPFC	-0.36	0.22	-0.40	0.11	0.05	0.84
HC	-0.12	0.64	0.05	0.84	-0.09	0.74
MPFC	-0.23	0.38	-0.29	0.26	0.03	0.92
Temporal cortex	-0.28	0.27	-0.25	0.33	0.05	0.84
GM	-0.27	0.29	-0.43	0.09	0.01	0.96
WB	-0.29	0.25	-0.42	0.10	-0.01	0.96
V_T with PVEC	**r**	**p**	**r**	**p**	**r**	**p**
DLPFC	-0.31	0.22	-0.36	0.16	0.03	0.91
HC	-0.13	0.61	0.05	0.86	-0.08	0.75
MPFC	-0.24	0.35	-0.25	0.33	0.02	0.95
Temporal cortex	-0.32	0.21	-0.23	0.39	0.05	0.86
GM	-0.25	0.33	-0.42	0.10	-0.00	0.99
WB	-0.26	0.31	-0.40	0.12	-0.01	0.98

Data was not available for one subject.

Abbreviations: DLPFC, dorsolateral prefrontal cortex; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; MPFC, medial prefrontal cortex; ; ROI, region of interest; SE, standard error; WB, whole brain.

TABLE S10. Association between [^{18}F]FEPPA V_T and PANSS scores in first episode psychosis (n=15) after excluding n = 4 who had first episode more than 5 years before scanning, adjusted for TSPO genotype (rs6971).

V_T	Positive		Negative		General		Total	
ROI	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
DLPFC	-0.18	0.54	-0.05	0.87	-0.43	0.13	-0.30	0.30
HC	-0.24	0.41	-0.11	0.70	-0.48	0.08	-0.38	0.19
MPFC	-0.15	0.60	-0.16	0.59	-0.48	0.08	-0.37	0.19
Temporal cortex	-0.24	0.42	-0.17	0.56	-0.47	0.09	-0.40	0.16
GM	-0.27	0.35	-0.12	0.69	**-0.57**	**0.03**	-0.44	0.12
WB	-0.34	0.24	-0.10	0.74	-0.61	0.20	-0.47	0.09
V_T with PVEC	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
DLPFC	-0.11	0.71	-0.12	0.69	-0.42	0.13	-0.31	0.28
HC	-0.18	0.54	-0.12	0.69	-0.46	0.10	-0.35	0.22
MPFC	-0.10	0.75	-0.18	0.53	-0.43	0.12	-0.34	0.23
Temporal cortex	-0.14	0.63	-0.17	0.55	-0.42	0.13	-0.35	0.23
GM	-0.22	0.46	-0.15	0.61	**-0.56**	**0.04***	-0.42	0.13
WB	-0.20	0.48	-0.12	0.70	**-0.54**	**0.05***	-0.40	0.16

* *$p<0.05$; adjusted p-value threshold: $p<0.017$ for PANSS subscales*

Abbreviations: DLPFC, dorsolateral prefrontal cortex; FEP, first episode of psychosis; GM, gray matter; HC, hippocampus; MPFC, medial prefrontal cortex; ; ROI, region of interest; SE, standard error; WB, whole brain.

3. Supplemental Figures

FIGURE S1. Total distribution volume of [^{18}F]FEPPA (V_T) in psychotic patients (FEP) and healthy volunteers (HV) across different regions of interest (dorsolateral prefrontal cortex, dorsolateral prefrontal cortex, DLPFC; hippocampus, HC; Medial prefrontal cortex, mPFC; Temporal cortex; total gray matter, GM; whole brain, WB) after correction for partial volume effect (PVEC).

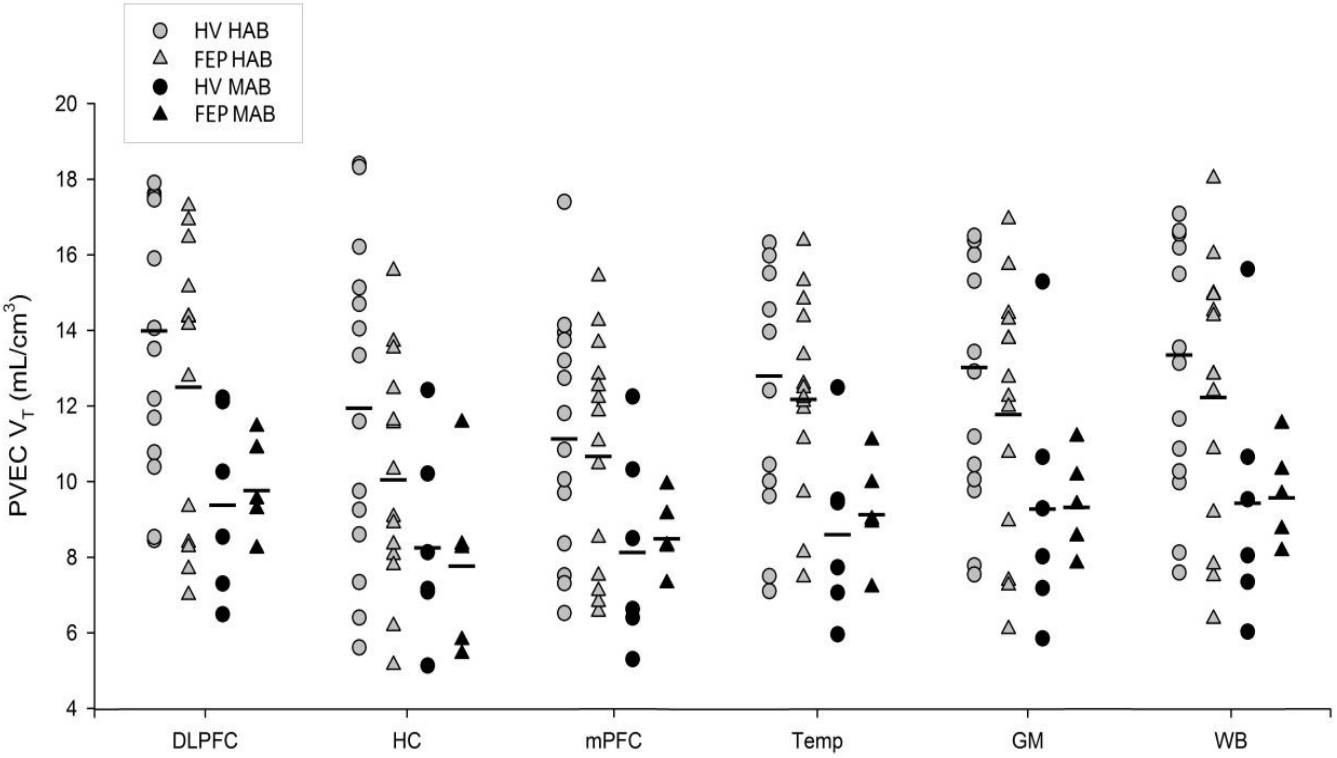


FIGURE S2. t-statistical maps of parametric images of [^{18}F]FEPPA total distribution volume (V_T) overlaid on T1-weighted magnetic resonance imaging (MRI) template. TSPO genotype (rs6971) was added as covariate. Voxel threshold was set to *p*< 0.05 (FWE corrected).

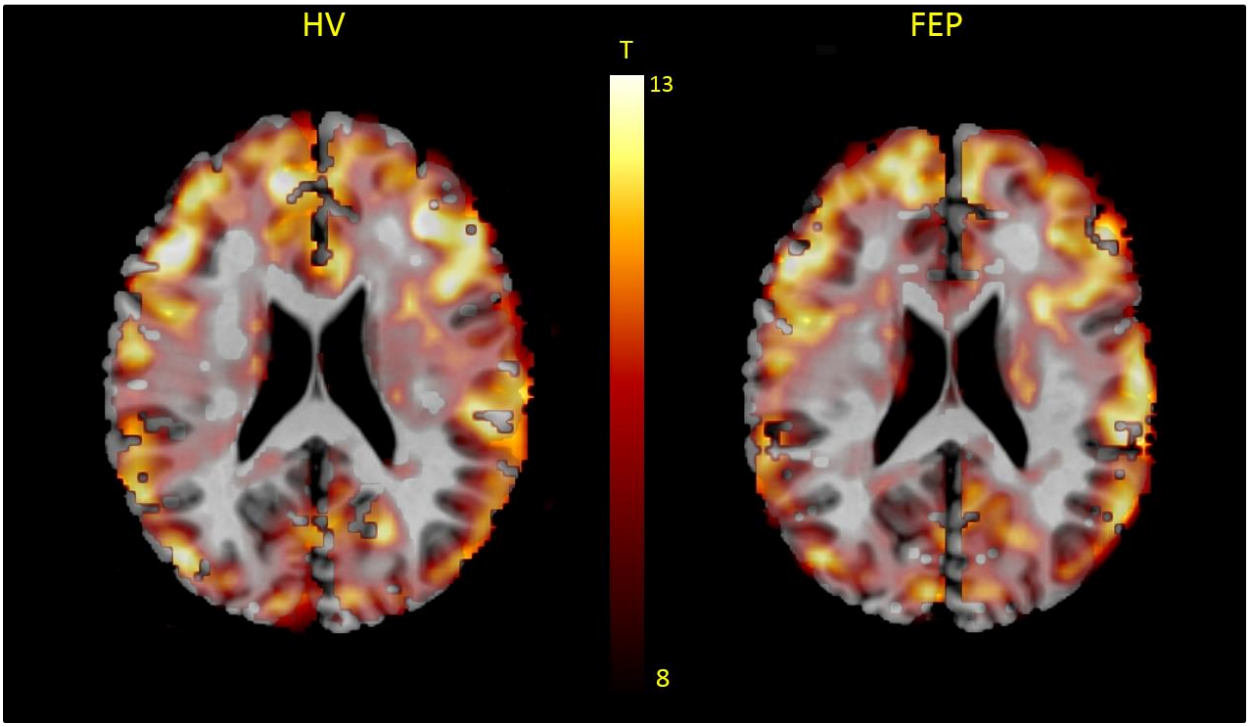
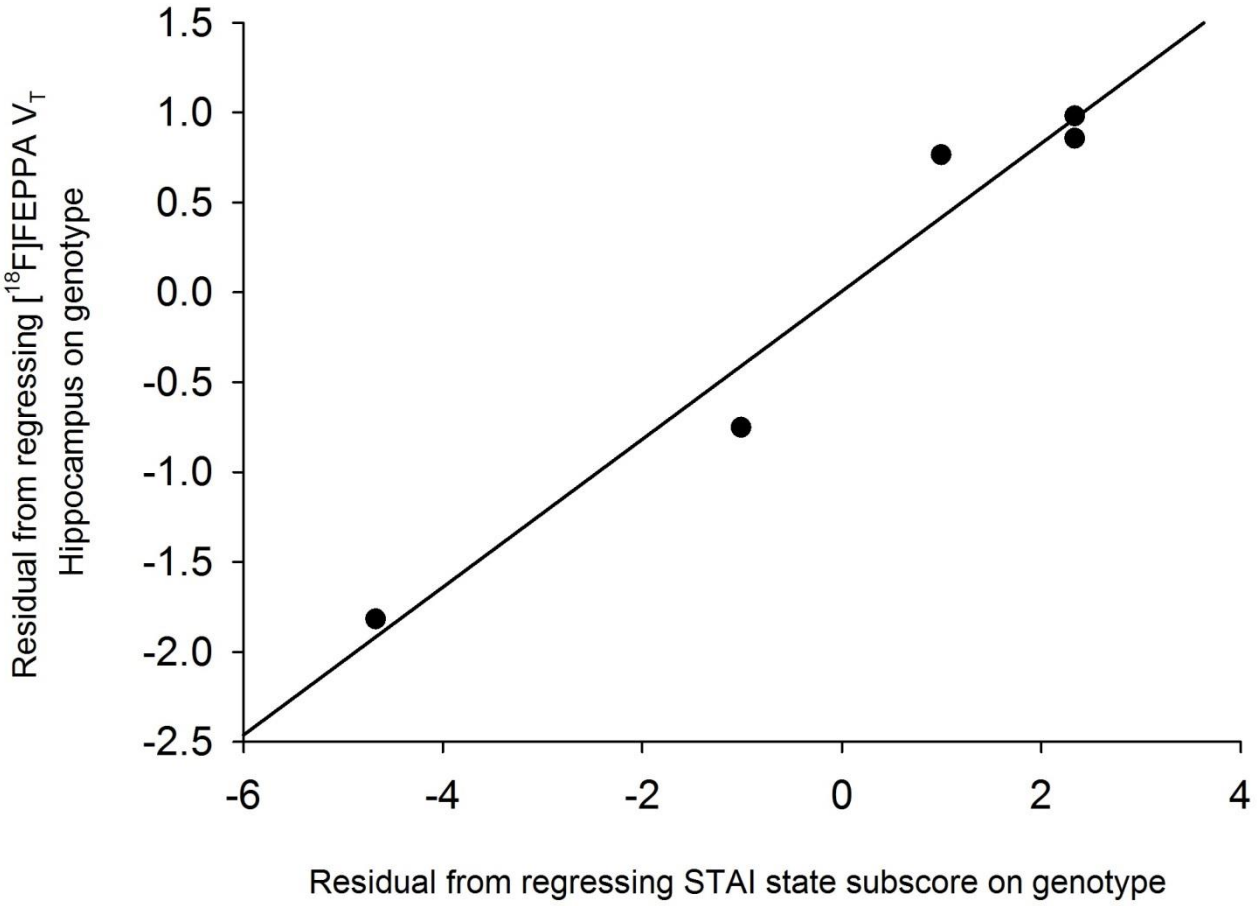


FIGURE S3. Partial correlation between [^{18}F]FEPPA V_T and the State-Trait Anxiety Inventory (STAI)(22) score controlling for TSPO genotypes (rs6971). A significant positive association between [^{18}F]FEPPA V_T of hippocampus and the score of STAI State subscale (r = .98, p = .02). Caution should be exercised due to very small n.



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