SUPPLEMENTAL METHODS

Safety monitoring

Subjects were monitored for changes in blood pressure, temperature, heart rate, respiration rate, and electrocardiogram tracing were monitored before and after injection of [^{11}C]PBR28. Blood and urine laboratory tests were repeated within 24 hours after completion of the study.

Brain scan acquisition

After an 8-min ^{68}Ge transmission scan was performed for attenuation correction, [^{11}C]PBR28 was injected as an intravenous bolus. The PET scan was acquired in 3D dynamic mode using a GE Advance tomograph (GE Medical Systems, WI) for total scan time of either 90 or 120 min.

Arterial blood was manually sampled at 15 s intervals for first 2 ½ min, then at 3, 4, 6, 8, 10, 15, 20, 30, 40, 50, 60, 75, and 90. Radioactivity in plasma was quantified by a γ-counter and analyzed by reverse-phase chromatography to separate parent radioligand from radiometabolites (Zoghbi et al. 2006). Free fraction of [^{11}C]PBR28 in plasma (f_P) was measured by ultrafiltration and normalized using a standard derived from pooled donor plasma (Abi-Dargham et al. 1995).

Image analysis

Image and kinetic analyses were performed using PMOD 2.95 (pixel-wise modeling software; PMOD Technologies Ltd., Adliswil, Switzerland). PET data were corrected for attenuation and scattered radiation, and were reconstructed on a 128 × 128 matrix with a pixel size of 2.0 × 2.0 × 4.25 mm in the x, y, and z axis, respectively. PET images from each subject

were then realigned using Statistical Parametric Mapping 5 (SPM 5; Wellcome Department of Cognitive Neurology, London, UK) to correct for head movement, and were averaged to create images with good delineation of cerebral cortices. Using SPM5, each subject's MR image was coregistered to their average PET image, and the MR and all PET images were spatially normalized to a standard space (Montreal Neurological Institute). Volumes of interest (VOI) were placed on the spatially normalized PET images overlying the frontal, parietal, occipital, temporal, medial temporal, and cingulate cortices. A weighted average of counts from these regions was used to great whole brain VOI.

Time-activity data were analyzed with the two-tissue compartment models, using the radiometabolite-corrected plasma input function. The input function was calculated as linear interpolation of the concentrations of [^{11}C]PBR28 before the peak, and a tri-exponential fit of concentrations after the peak. Brain data of each frame were weighted relative to other frames by assuming that the standard deviation of the data was proportional to the inverse square root of noise equivalent counts. Time-activity data was corrected for activity in the cerebral blood volume, which was assumed to be 5% of brain volume. Total distribution volume (V_T, mL / cm^3) was calculated for each VOI.

REFERENCES

Abi-Dargham A, Gandelman M, Zoghbi SS, Laruelle M, Baldwin RM, Randall P, Zea-Ponce Y, Charney DS, Hoffer PB, Innis RB. (1995) Reproducibility of SPECT measurement of benzodiazepine receptors in human brain with iodine-123-iomazenil. *J Nucl Med* 36:167-175

Zoghbi SS, Shetty HU, Ichise M, Fujita M, Imaizumi M, Liow JS, Shah J, Musachio JL, Pike VW, Innis RB. (2006) PET imaging of the dopamine transporter with [^{18}F]FECNT: a polar radiometabolite confounds brain radioligand measurements. *J Nucl Med* 47:520-527

Supplemental Table 1. Characteristics of subjects in [^{3}H]PBR28 in vitro binding study.

	Controls			Schizophrenia		
	HH	HL	LL	HH	HL	LL
Gender						
Male	17	9	4	14	8	1
Female	12	4	1	12	9	1
Race						
African American	19	9	1	14	13	0
Caucasian	9	4	4	10	4	2
Hispanic	1	0	0	1	0	0
Age at Death (years)*	42	40	58	55	56	71
Age of Onset of Illness	NA	NA	NA	24	25	26
Duration of Illness (years)	NA	NA	NA	32	32	18
Brain pH*	6.49	6.66	6.70	6.24	6.21	6.40
Postmortem Interval (hours)	35.2	37.0	45.2	45.4	33.7	38.0
Body Mass Index	31.8	29.5	30.3	30.2	30.1	23.8
Brain Weight (g)*	1 348	1 432	1 478	1 314	1 260	1 255
Time Frozen (years)*	9.65	11.04	6.51	7.85	8.43	7.98
Manner of Death						
Natural	22	10	4	20	14	1
Accidental	3	3	1	3	1	1
Homicide	4	0	0	0	0	0
Suicide	0	0	0	2	2	0
Undetermined	0	0	0	1	0	0
Substance use						
Habitual Smoker at time of death*	9	4	1	18	16	1
Comorbid Alcohol Abuse / Dependence	0	0	0	3	8	0
Comorbid Substance Abuse / Dependence	0	0	0	7	0	0
THC or Metabolites in Toxicology	0	0	0	0	0	1
Nicotine*	7	3	0	11	5	1
Chlorpromazine Equivalents						
Last Dose (mg / d)	NA	NA	NA	842 ± 633	612 ± 649	200
Average Daily Dose (mg /d)	NA	NA	NA	708 ± 435	481 ± 339	800
Lifetime Dose (g)	NA	NA	NA	6 812 ± 4 899	4 820 ± 3 145	7 884

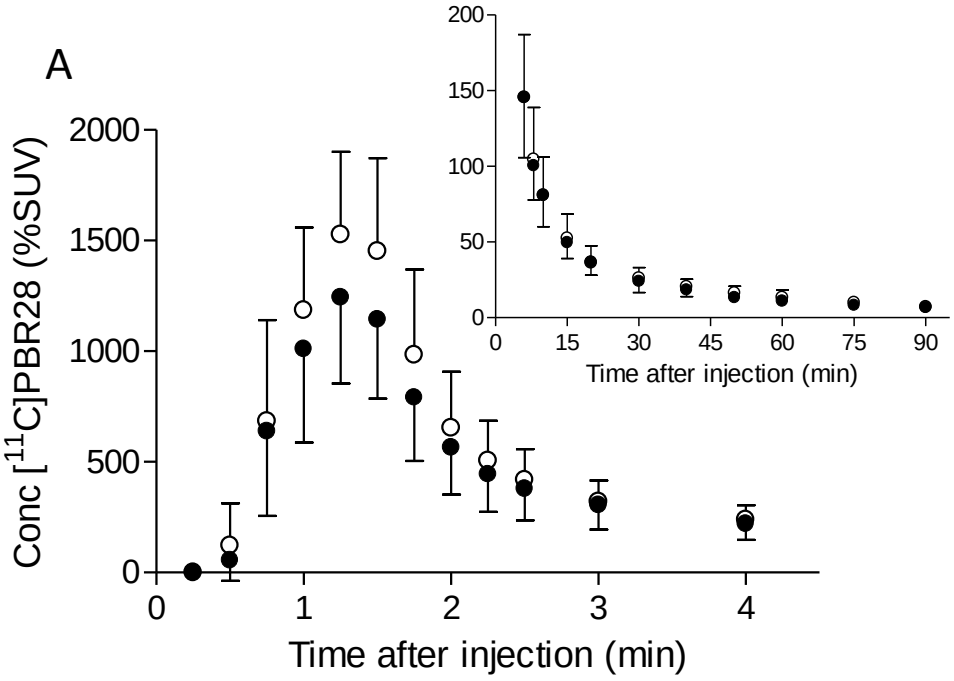
* $p < 0.05$ in healthy controls vs. schizophrenia patients.

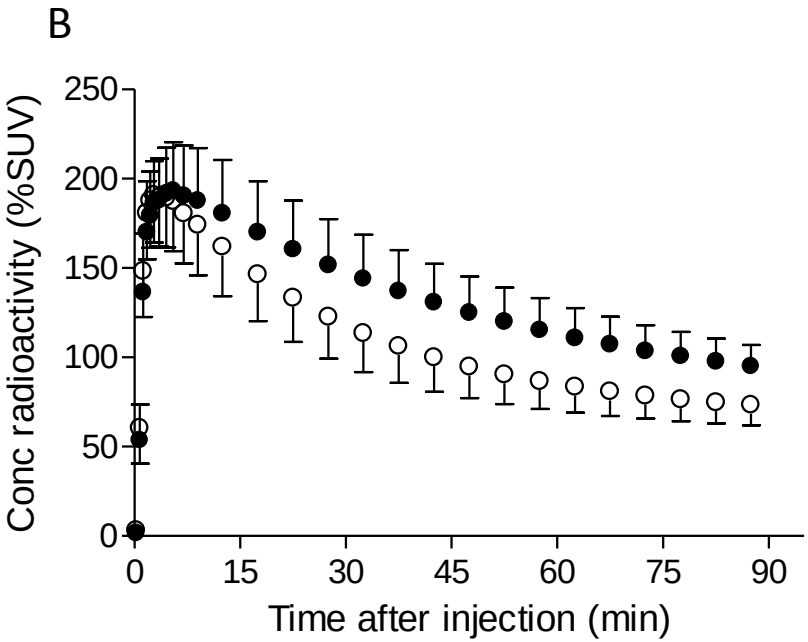
NA = Not applicable.

Supplemental Table 2. Demographic characteristics of subjects who underwent [^{11}C]PBR28 PET.

Binding affinity	Gender (F, M)	Race (AA, AS, C, L)	Age (years)	weight (kg)
HH	4, 5	5, 0, 4, 0	45.2 ± 15.2	88.4 ± 17.3
HL	7, 11	2, 1, 14, 1	45.9 ± 19.6	81.6 ± 16.3

HH = high affinity binder, HL = mixed affinity binder, F = female, M = male,
AA = African-American, AS = Asian, C = Caucasian, L = Latino.
Some data given as mean ± SD.


A
Conc [11C]PBR28 (%SUV)
2000
1500
1000
500
0
0
1
2
3
4
Time after injection (min)
200
150
100
50
0
0
15
30
45
60
75
90
Time after injection (min)


B
Conc radioactivity (%SUV)
250
200
150
100
50
0
0
15
30
45
60
75
90
Time after injection (min)