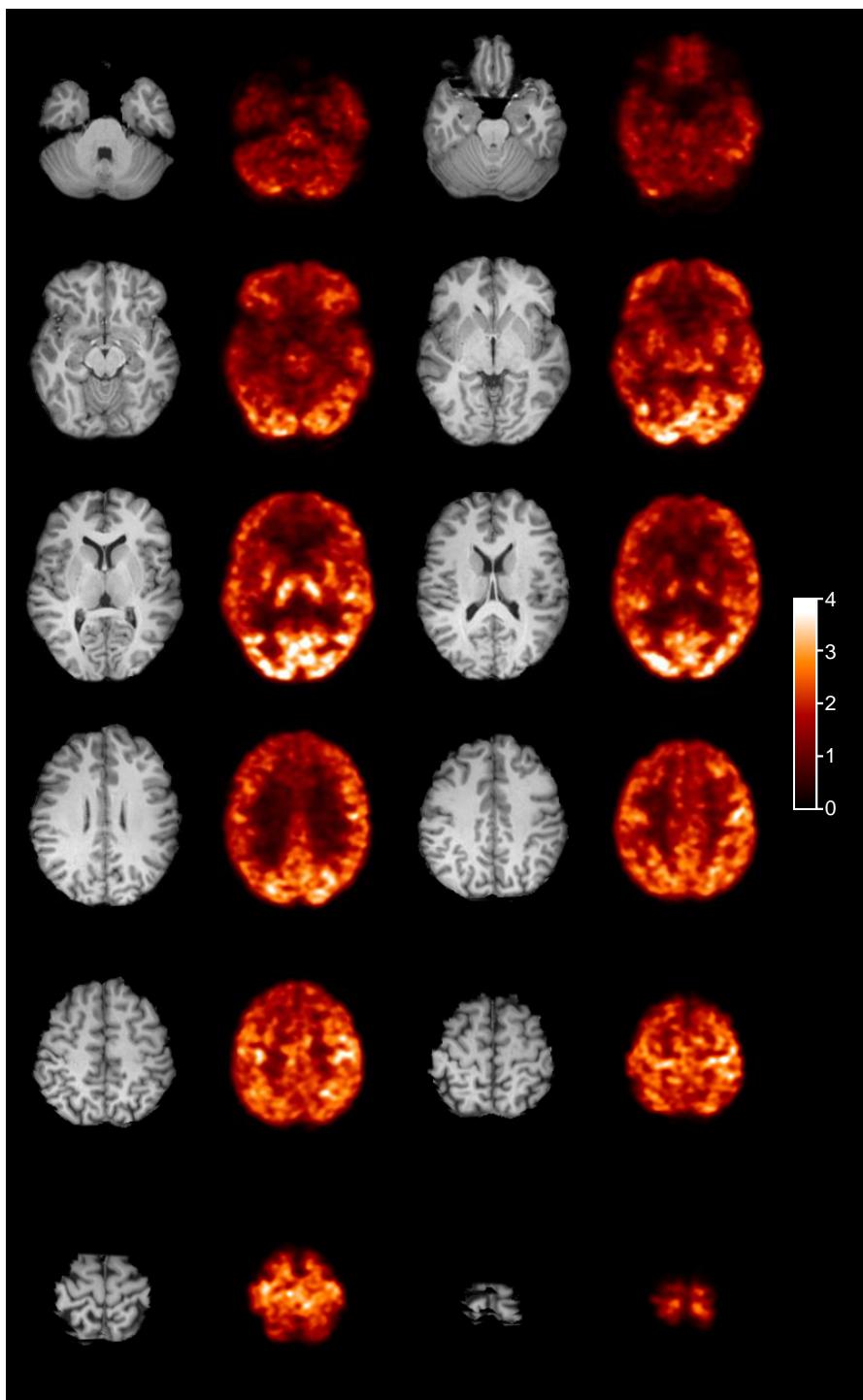
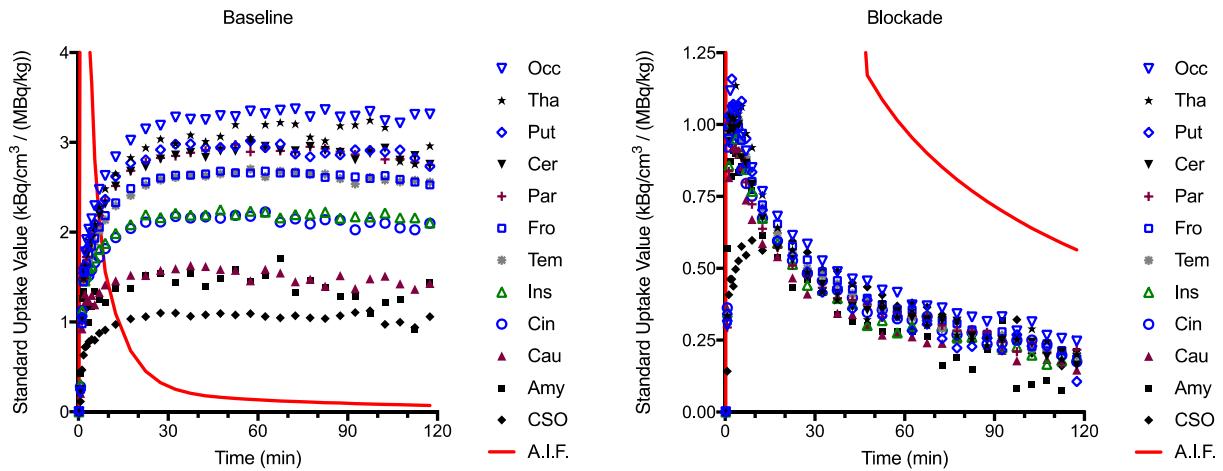


**Supplemental Figure 1:** Parent fraction in plasma for the baseline or test scans (n=15, black), blockade scans (n=2, red), and retest scans (n=5, blue). Data are presented as mean  $\pm$  standard deviation. Error bars are not shown if they are shorter than the symbol used to show the mean.



**Supplemental Figure 2:** Transverse PET slices from a baseline  $^{11}\text{C}$ -AS2471907 scan, shown as standard uptake values (SUV, averaged from 40-60 min post injection). Corresponding MR images are shown to the left-hand side of each PET image.



**Supplemental Figure 3:** Representative brain time-activity curves at baseline and after pre-blockade of 11 $\beta$ -HSD1 binding sites with ASP3662. Occ = Occipital Cortex, Tha = Thalamus, Put = Putamen, Cer = Cerebellum, Par = Parietal Cortex, Fro = Frontal cortex, Tem = Temporal cortex, Ins = Insula, Cin = Cingulum, Cau = Caudate Nucleus, Amy = Amygdala, CSO = Centrum Semiovale, A.I.F. = Metabolite-Corrected Arterial Input Function.

**Supplemental Table 1:** 2TC  $V_T$  values estimated for the baseline and blockade scans.

	Subject 6		Subject 7	
	Baseline	Blockade	Baseline	Blockade
Caudate Nucleus	7.2	0.20	2.4	0.13
Amygdala	6.6	0.17	4.2	0.16
Centrum Semiovale	6.1	0.25	3.1	0.18
Cingulum	13.4	0.22	4.3	0.15
Insula	14.7	0.22	3.9	0.15
Frontal Cortex	18.5	0.24	5.3	0.17
Putamen	19.1	0.22	6.1	0.15
Temporal Cortex	20.7	0.23	5.4	0.16
Parietal Cortex	22.4	0.23	6.8	0.18
Cerebellum	23.6	0.24	4.8	0.14
Thalamus	27.1	0.25	9.1	0.16
Occipital Cortex	28.3	0.28	9.8	0.19

**Supplemental Table 2:** 2TC  $V_T$  values estimated from the test and retest scans.

Subject	Scan	Injection Time	CSO	Amy	Cau	Put	Tha	Cer	Cin	Ins	Fro	Occ	Par	Tem
1	T	10:46	6.8	3.1	3.6	7.1	13.5	6.1	5.2	4.9	6.4	11.1	10.4	6.2
1	R	15:43	4.8	2.4	3.4	9.5	11.0	5.8	6.9	5.7	7.4	11.4	10.5	7.4
2	T	10:47	5.0	4.3	4.2	9.5	9.6	5.8	6.8	6.7	9.0	14.9	11.1	9.0
2	R	17:12	7.5	3.5	4.7	10.7	12.7	7.7	8.1	8.7	10.4	17.7	12.9	11.5
3	T	12:18	4.9	8.2	6.6	11.3	15.8	19.0	8.8	8.2	12.2	20.9	14.9	13.3
3	R	16:44	5.4	5.2	10.7	11.3	17.6	20.0	9.3	8.8	12.6	23.4	20.4	14.1
4	T	09:48	2.3	1.3	2.2	4.4	9.2	6.5	3.4	3.5	4.4	7.8	5.5	4.7
4	R	14:50	3.1	3.0	2.1	5.2	12.6	6.4	4.2	4.1	5.0	9.0	6.7	5.4
5	T	15:02	4.5	7.8	3.6	13.4	14.6	8.6	7.7	8.1	11.0	17.3	13.7	10.8
5	R	17:45	5.0	5.8	4.0	12.7	16.3	10.3	9.0	8.5	11.3	19.2	13.6	11.5

T = Test, R = Retest, CSO = Centrum Semiovale, Amy = Amygdala, Cau = Caudate Nucleus, Put = Putamen, Tha = Thalamus, Cer = Cerebellum, Cin = Cingulum, Ins = Insula, Fro = Frontal cortex, Occ = Occipital Cortex, Par = Parietal Cortex, Tem = Temporal cortex.

**Supplemental Table 3:** Bias\* on 2TC  $V_T$  values estimated with shorter scan length.

Scan length (min)	60	70	80	90	100	110
Caudate Nucleus	817% $\pm$ 3592%	39% $\pm$ 110%	13% $\pm$ 23%	11% $\pm$ 19%	9% $\pm$ 12%	5% $\pm$ 5%
Amygdala	12% $\pm$ 61%	9% $\pm$ 39%	6% $\pm$ 25%	7% $\pm$ 16%	5% $\pm$ 9%	4% $\pm$ 5%
Centrum Semiovale	12% $\pm$ 40%	8% $\pm$ 18%	9% $\pm$ 14%	6% $\pm$ 9%	4% $\pm$ 6%	2% $\pm$ 3%
Cingulum	5% $\pm$ 12%	6% $\pm$ 11%	5% $\pm$ 8%	5% $\pm$ 6%	4% $\pm$ 4%	2% $\pm$ 3%
Insula	4% $\pm$ 13%	6% $\pm$ 10%	5% $\pm$ 7%	5% $\pm$ 6%	4% $\pm$ 5%	2% $\pm$ 2%
Frontal Cortex	2% $\pm$ 12%	3% $\pm$ 9%	3% $\pm$ 7%	4% $\pm$ 5%	3% $\pm$ 4%	2% $\pm$ 2%
Putamen	7% $\pm$ 30%	7% $\pm$ 18%	4% $\pm$ 13%	3% $\pm$ 9%	4% $\pm$ 7%	2% $\pm$ 4%
Temporal Cortex	5% $\pm$ 16%	8% $\pm$ 14%	8% $\pm$ 11%	7% $\pm$ 9%	4% $\pm$ 5%	2% $\pm$ 3%
Parietal Cortex	9% $\pm$ 17%	8% $\pm$ 12%	8% $\pm$ 11%	7% $\pm$ 8%	4% $\pm$ 5%	2% $\pm$ 2%
Cerebellum	11% $\pm$ 29%	15% $\pm$ 26%	11% $\pm$ 20%	9% $\pm$ 17%	6% $\pm$ 9%	4% $\pm$ 4%
Thalamus	3% $\pm$ 12%	4% $\pm$ 11%	5% $\pm$ 8%	5% $\pm$ 7%	3% $\pm$ 4%	2% $\pm$ 3%
Occipital Cortex	28% $\pm$ 34%	23% $\pm$ 24%	17% $\pm$ 17%	14% $\pm$ 12%	10% $\pm$ 8%	5% $\pm$ 3%

\* Bias are computed as  $V_T^{Scan\ length}/V_T^{120\ min} - 1$ , and presented as mean  $\pm$  standard deviation.