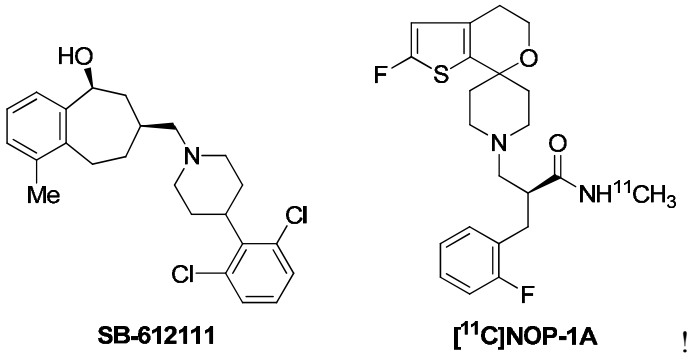
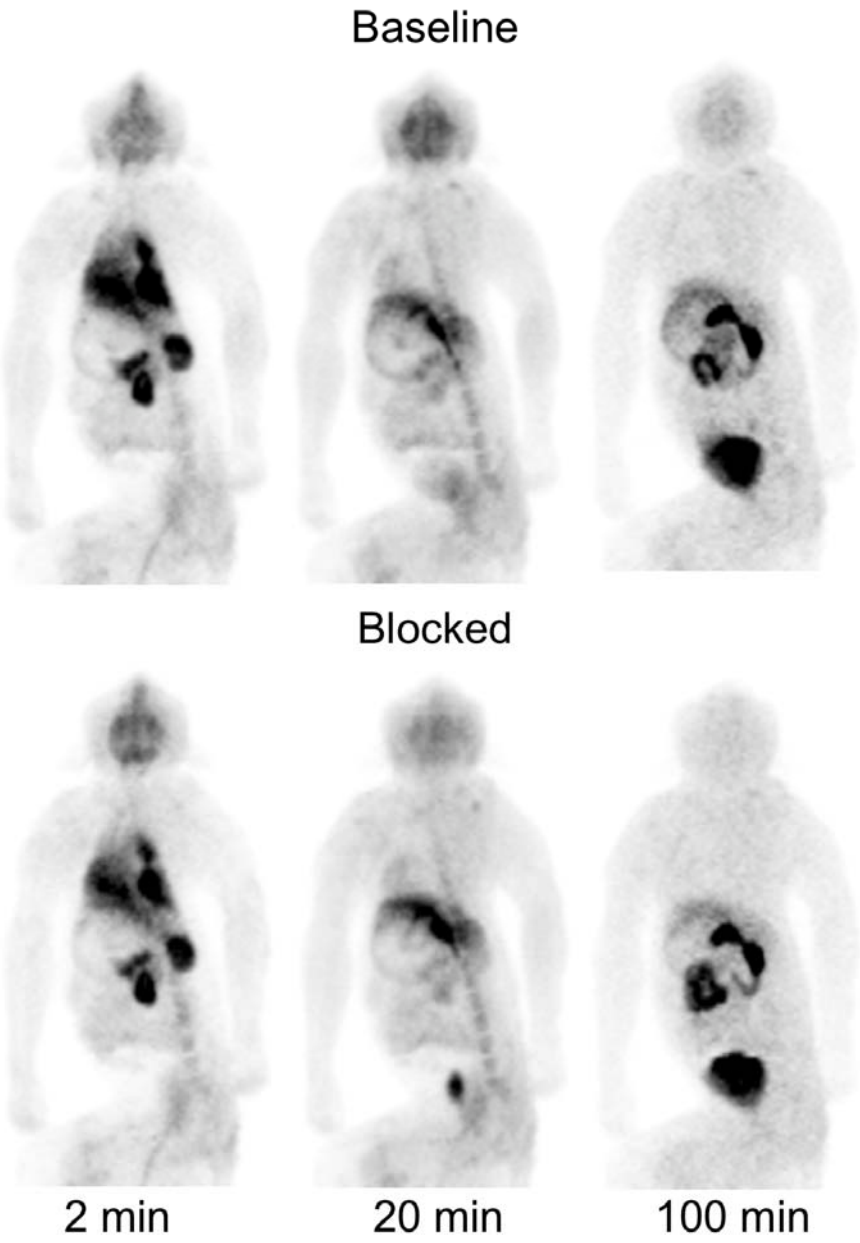
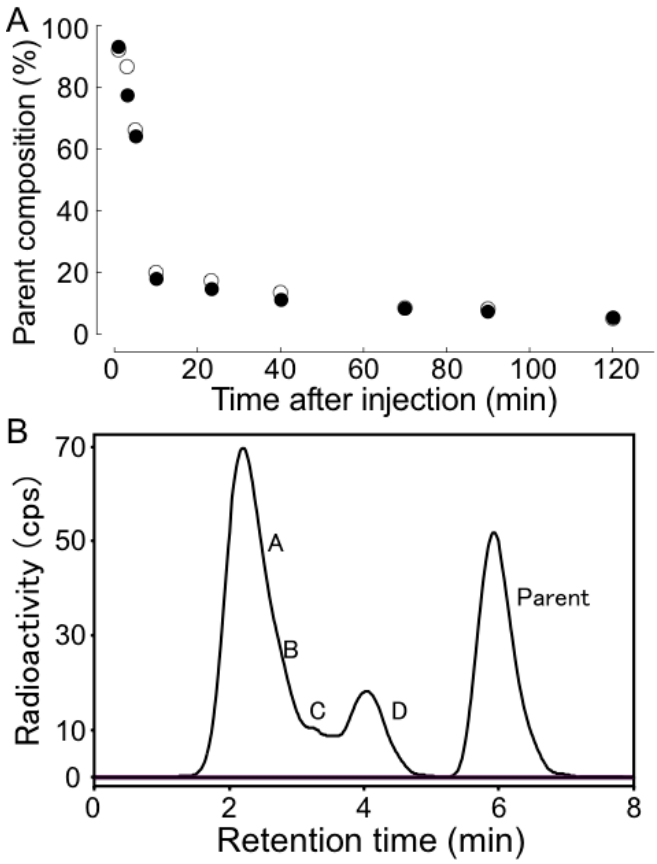


Supplemental Fig 1. Structures of NOP receptor ligands: SB-612111 and ^{11}C-NOP-1A.



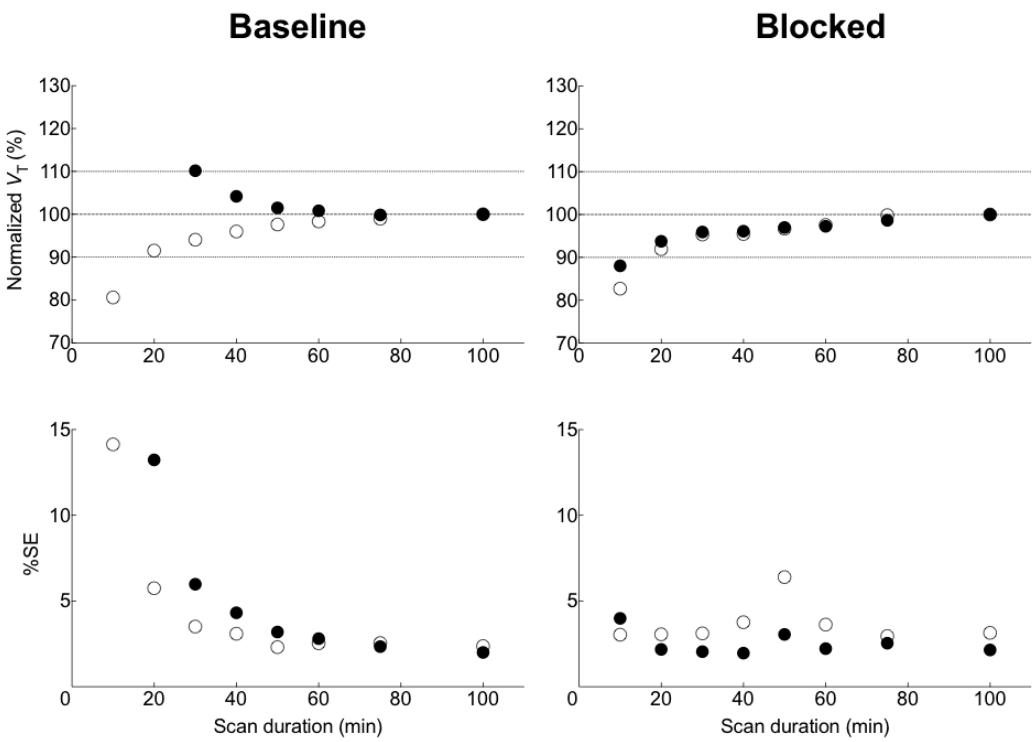
Supplemental Fig 2. **Whole-body images of the same monkey at 2, 20, and 110 minutes after ^{11}C-NOP-1A injection at baseline (top) and after receptor blockade with SB-612111 (bottom).** In addition to high uptake in brain, the image at 2 minutes shows high uptake in lungs, kidney, and heart. The image at 20 minutes shows particularly high uptake in vertebrae, and that at 110 minutes shows excretion of radioactivity via small bowel, urinary bladder, and liver/gallbladder. These images were created by summing all coronal slices at each time-point. The pixel values were decay-corrected to time of injection and displayed with the same gray scale.



Supplemental Fig 3. **Percent composition of plasma radioactivity after injection of ^{11}C-NOP-1A and a radiochromatogram of plasma at 30 minutes.**

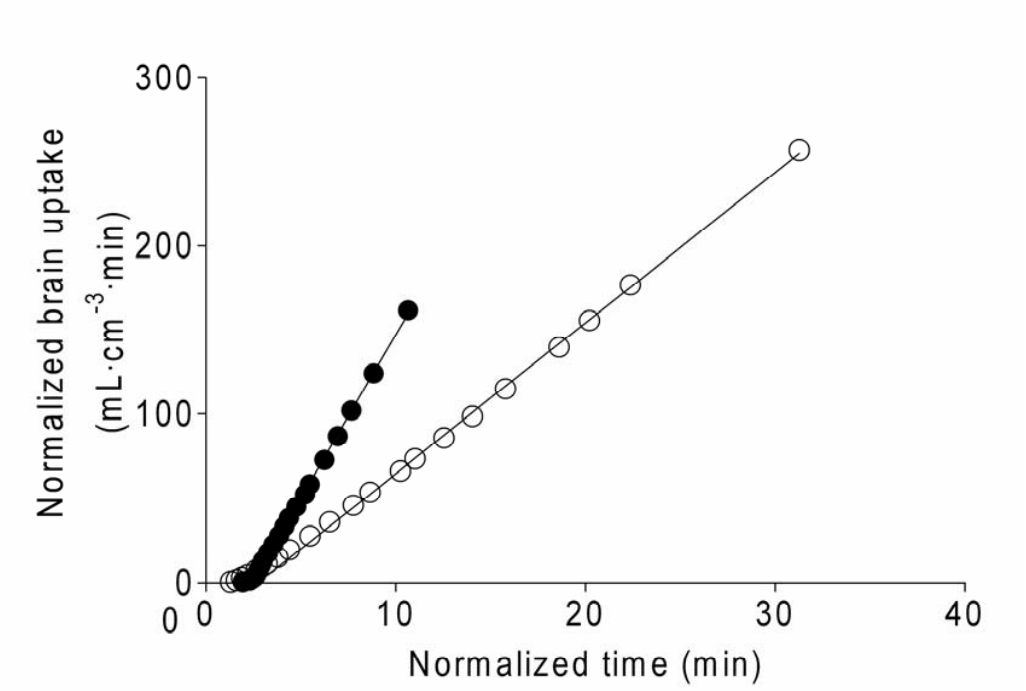
(A) The percent composition of plasma radioactivity after injection is plotted at baseline (●) and after receptor blockade with SB-612111 (○). Symbols are the percentage of total radioactivity in plasma that represents parent radioligand and are the mean of three determinations.

(B) Radiochromatogram of a 30-minute plasma sample collected after the intravenous injection of ^{11}C-NOP-1A (232 MBq) in a rhesus monkey. The most polar radiometabolites (A, B, and C) eluted within or near the void volume of the column and were not well resolved. Radiometabolite D was more lipophilic than the other radiometabolites but considerably less lipophilic than the parent radioligand. ^{11}C-NOP-1A was the most lipophilic peak, eluted at 6 minutes, and was well separated from all radiometabolites.



Supplemental Fig 4. **Value of V_T and identifiability (%SE) as function of duration of image acquisition at baseline and after receptor blockade with SB-612111 in three monkeys.**

V_T was calculated for occipital cortex (●) and cerebellum (○) using one-tissue compartment model. Scans were analyzed using brain data from time 0 to specified time on X-axis. V_T was expressed as percentage of the terminal value calculated from the entire 100-minute scan. The terminal value was plotted at 100 minutes because it was the mid-point of the last acquisition from 98 to 102 minutes for the bed position that included the brain. Normalized V_T values are shown for occipital cortex (●) and cerebellum (○) at baseline (left) and after receptor blockade (right) in the top tables. Corresponding values of identifiability (%SE) are shown in the bottom panels.



Supplemental Fig 5. Representative Logan plot of the data in the occipital cortex at baseline (●) and after receptor blockade (ʘ). The start time for the linear part of the Logan plotting varied among regions and monkeys but usually occurred between 5 and 44 minutes after injection of radioligand. In these data, the time for start of the linear analysis was 5 minutes in real time (2.6 minutes in normalized time) for the baseline scan and 23 minutes in real time (6.5 minutes in normalized time) for the receptor blocked scan. V_T, calculated as the slope of the linear portion of the curve, was 19.4 at baseline and 9.0 mL · cm^{-3} after blockade.

Supplemental Table 1 Scaling factors for organs in monkey and man were based on their percentage contribution to total body weight*.

Organ	% of Total Body Weight		Scaling Factor***
	Monkey	Human (*3*)	$(b_m/o_m) \times (o_h/b_h)$
Brain (*1*)	1.4%	2.0%	1.41
Heart wall (with blood) (*1*)	0.4%	1.2%	2.60
Lung (with blood) (*1*)	0.8%	1.6%	1.96
Liver (*1*)	2.3%	2.5%	1.05
Gallbladder**	0.0%	0.0%	0.98
Spleen (*1*)	0.1%	0.2%	2.75
Kidney (*1*)	0.4%	0.4%	1.09
Cortical bone (*2*)	2.9%	6.0%	2.07
Trabecular bone (*2*)	1.0%	1.5%	1.49
Small intestine†(*1*)	2.3%	0.9%	0.39
Upper large intestine† (*1*)	0.5%	0.2%	0.39
Lower large intestine† (*1*)	0.5%	0.2%	0.39
Urinary bladder‡	0.1%	0.1%	1.00
Remainder of body	84.9%	78.2%	0.92

* Garth Terry, MD, PhD created this Table while a graduate student in Dr. Innis's laboratory in the NIH / Karolinska Institutet Doctoral Program in Neuroscience.

**Gallbladder was estimated from proportion of gallbladder/(liver plus gallbladder) in human, as gallbladder weight was recorded together with liver in monkey.

†Proportions for small intestine, upper large intestine, and lower large intestine were taken from human, because only total intestine weight was reported for monkey.

‡Urinary bladder is not available for monkey; equal proportions were assumed.

***The scaling factor was multiplied by the residence time determined from monkey to estimate its value in humans. The factor corrected for varying percentage of total body weight in each organ, where b_m and b_h are the body weights of monkey and human, respectively, and o_m and o_h are the organ weights of monkey and human, respectively.

References for Supplemental Table 1.

1. Bourne GH. *The Rhesus Monkey: Anatomy and physiology*. Burlington, MA: Academic Press; 1975.

2. Gong JK. Volumetric composition of the monkey skeleton. *Anat Rec*. 1972;172:543-550.

3. The International Commission on Radiological Protection. Basic anatomical and physiological data for use in radiological protection: reference values. ICRP Publication 89. *Ann ICRP.* 2002;32:1–277.

Supplemental Table 2. Residence times of source organs determined from whole-body imaging of three monkeys injected with ^{11}C-NOP-1A.

Organs	Residence time (h)
Brain	0.023
Total Red marrow	0.029
Liver	0.075
Gall Bladder	0.014
Small intestine	0.006
Kidney	0.013
Urinary Bladder	0.021
Lung	0.039
Spleen	0.007
Heart	0.013
Reminder of the body	0.250

Values are mean from three monkeys