SUPPLEMENTARY INFORMATION

Supplementary Methods

PET experiments under anesthesia. In order to assess the effects of anesthetics, we conducted PET scans for a monkey unanesthetized and anesthetized with ketamine (3.75 mg/kg/h i.m.) and xylazine (1.5 mg/kg/h i.m.) and 3 rats unanesthetized and anesthetized with ketamine (45 mg/kg/h i.v.) and xylazine (6.0 mg/kg/h i.v.). Protocols for PET measurements and image analyses were identical to those described in Materials and Methods.

Supplementary microdialysis assays. Microdialysis assay of extracellular dopamine levels was performed for rats (n = 3) before and during treatment of ketamine (45 mg/kg/h i.v.). Similarly, rats (n = 2 in each treatment group) were analyzed by microdialysis along the course of treatment with either phencyclidine (3 mg/kg/h i.v.) or MPEP (1 mg/kg i.v.) followed by phencyclidine (1 mg/kg i.v.). Other assay protocols were identical to those described in Materials and Methods.
Legends for Supplementary Figures

Supplementary Figure 1. Influences of anesthetics on radiotracer kinetics and dopamine release in the striatum. (A and B) Striatal (circles) and cerebellar (squares) average time-radioactivity curves obtained from a monkey (A) and 3 rats (B) in awake (open symbols) and anesthetized (closed symbols) conditions. Data are expressed as % SUV, and bars represent SE.

Supplementary Figure 2. Recording of AMPA receptor-mediated EPSCs in MS neurons and effects of dopamine receptor blockade on methamphetamine-(MAP-)induced modulation of EPSCs. (A) A schematic representation of a brain slice containing the cortex and striatum that shows the position of the recording and stimulation pipettes. (B) Superimposed voltage responses from MS neurons in response to 1,000 ms hyperpolarizing and depolarizing currents. Calibration: 20 mV, 200 ms. (C) Effect of CNQX (20 μM; filled bar), AMPA receptor antagonist, on EPSCs recorded from MS neuron by stimulation on the subcortical white matter at a holding potential of -70 mV in the presence of picrotoxin. Traces 1-3, taken at indicated time points (red circles), are representative EPSCs before, during and after the application of CNQX, respectively. (D, E, F) Effect of dopamine D_{2/3} receptor selective antagonist sulpiride (10 μM; D), D_{1/5} receptor antagonist SCH23390 (10 μM; E) and their mixture (F) on the MAP-induced inhibition of EPSCs. (G) Summary of MAP-induced inhibition of EPSCs. Control data correspond to those in Fig. 6A, and other estimates are obtained from experiments shown in D, E and F. **p < 0.01 vs. control by unpaired Student’s t-test.
Supplementary Figure 3. Microdialysis assay of extracellular dopamine (DA) concentration in the striatum of rats. (A) Measurements in rats (n = 3) before and during ketamine treatment (horizontal bar, 45 mg/kg/h i.v.). (B) Assays in rats (n = 2 in each treatment group) along the course of phencyclidine (PCP) treatment (horizontal bar, 3 mg/kg/h i.v.) and combined MPEP and PCP administration (MPEP + PCP). Vertical bars represent SD.