

Figure S1, related to Fig. 3. S1a. Synaptic currents activated by 40 Hz, 5 pulse electrical stimulation in the ventral tegmental area are mediated by GABA<sub>B</sub> receptors. Outward currents elicited by electrical stimulation are completely inhibited by the selective GABA<sub>B</sub> receptor antagonist CGP55845 (10 μM). S1b. Bath application of cocaine (10 μM) reversibly inhibits GABA<sub>B</sub> IPSCs in putative VTA dopamine neurons. The time course of the effect of cocaine in 7 putative dopamine neurons is shown. Cocaine application is indicated by the shaded gray area. S1c. Averaged GABA<sub>B</sub> IPSC waveforms (n = 3-5 individual sweeps) showing the effects of cocaine as indicated in S1b. Scale bar, 100 ms, 10 pA (S1a), and 100 ms, 20 pA (S1c).

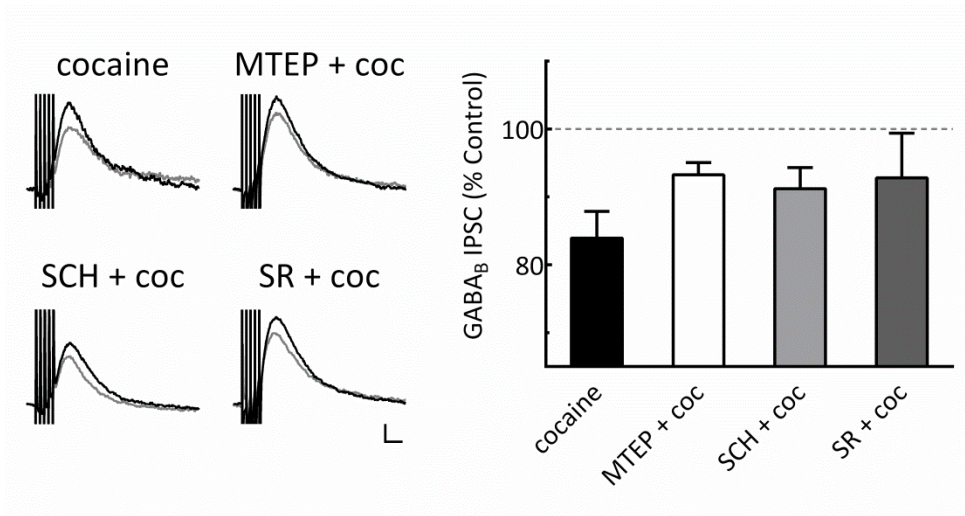


Figure S2, related to Fig. 5. Antagonists of mGluR5, DA-D<sub>1</sub>, and Neurotensin NTS<sub>1</sub> receptors do not significantly affect the inhibition of GABA<sub>B</sub> IPSC by cocaine. *Left*: Sample traces show the GABA<sub>B</sub> IPSC before (black) and after (gray) cocaine perfusion under different drug treatments. Scale bar: 10 pA, 100 ms. *Right*: summary the effects of cocaine with receptor antagonists. Cocaine (coc, 10 μM): 83.94 ± 3.91% of control, n = 10; MTEP (mGluR5 antagonist, 1 μM) + cocaine: 93.27 ± 1.79% of control, n = 8; SCH39166 (SCH, DA-D<sub>1</sub> antagonist, 1 μM) + cocaine: 91.21 ± 3.13% of control, n = 7; SR48692 (SR, neurotensin NTS<sub>1</sub> antagonist, 500 nM) + cocaine: 92.81 ± 6.59% of control, n = 5. F (3, 26) = 1.523, p = 0.23, one-way ANOVA.

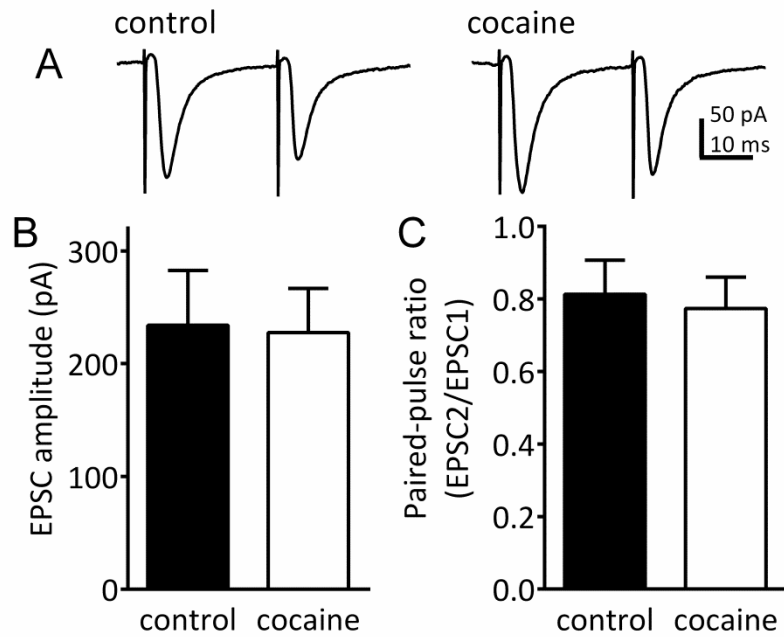


Figure S3, related to Fig. 5. Cocaine does not alter evoked glutamatergic EPSCs. A. Sample traces of evoked EPSCs before and after cocaine perfusion. Paired-pulse stimulation were delivered by two identical electrical stimulations ( $100 \mu\text{m}$ , 20-60 pA) separated by 25 ms. The 5-HT<sub>1B</sub> antagonist GR55562 ( $1 \mu\text{M}$ ) was in bath throughout the recording. B. The amplitudes of EPSCs are not changed by cocaine (control:  $234.0 \pm 48.7$  pA; cocaine:  $227.7 \pm 39.1$  pA;  $n = 8$ ;  $p = 0.62$ , paired  $t$ -test). C. The EPSC paired-pulse ratio (EPSC2/EPSC1) is not changed by cocaine (control:  $0.81 \pm 0.09$ ; cocaine:  $0.77 \pm 0.09$ ;  $n = 8$ ;  $p = 0.17$ , paired  $t$ -test).

Movie S1 (Related to Fig. 6): Cocaine-induced changes in calcium levels in VTA DA neurons measured by confocal imaging of GCaMP6f in vitro. Horizontal VTA slices were cut 18 days after AAV1.Syn.Flex.GCaMP6f injection. Confocal images were taken at 0.5 Hz with a 20x objective. Spontaneous calcium changes were monitored for 5 min before cocaine was applied for 20 min (indicated in movie). Image stacks were processed offline using the StackReg plug-in of ImageJ, and corrected for x-y drift. The video rate is 40x faster than actual time. Neurons whose calcium signals were decreased by cocaine are marked by blue arrow heads, whereas neurons showing initiation of slow calcium oscillation after cocaine application are marked by yellow arrow heads.