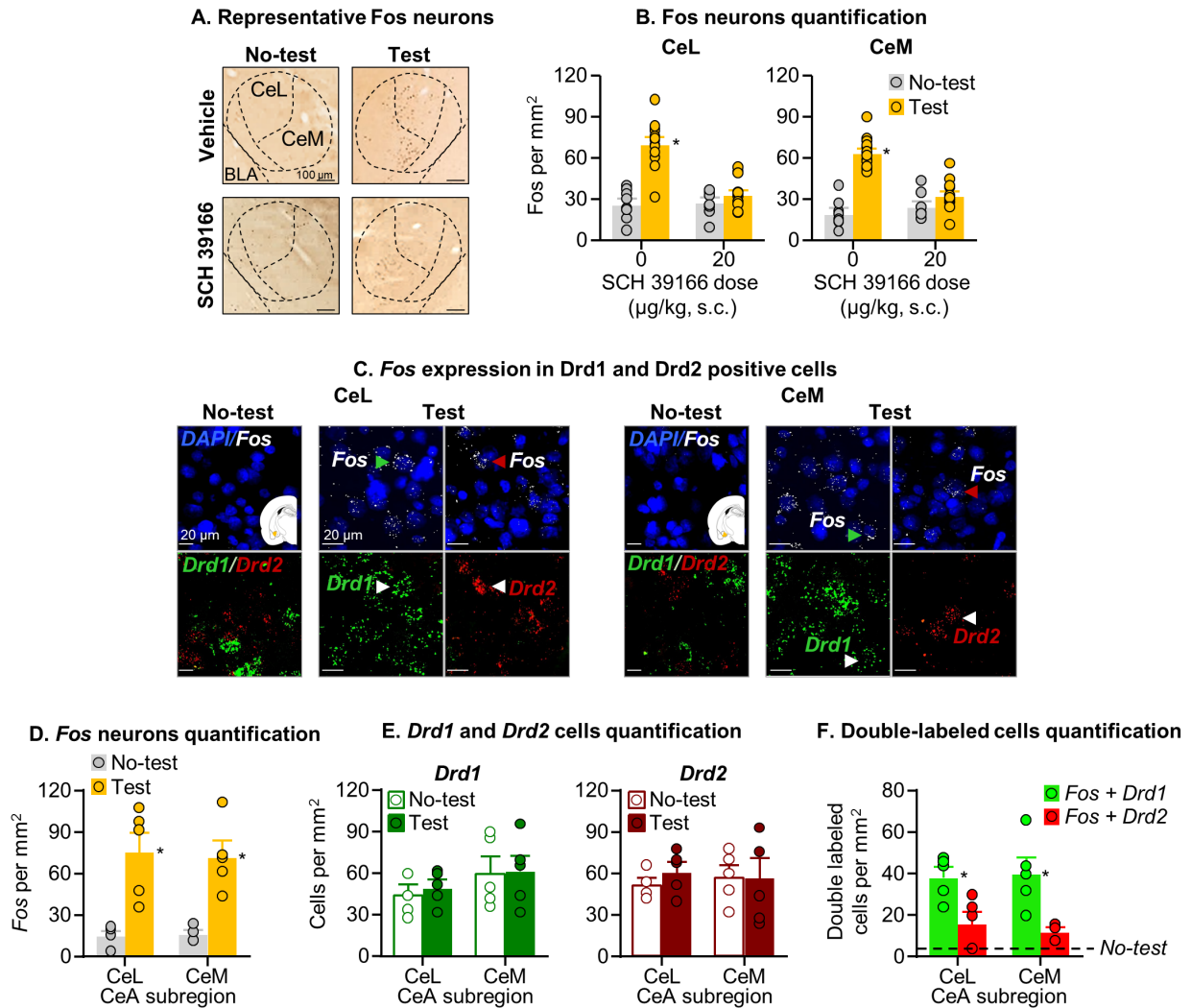
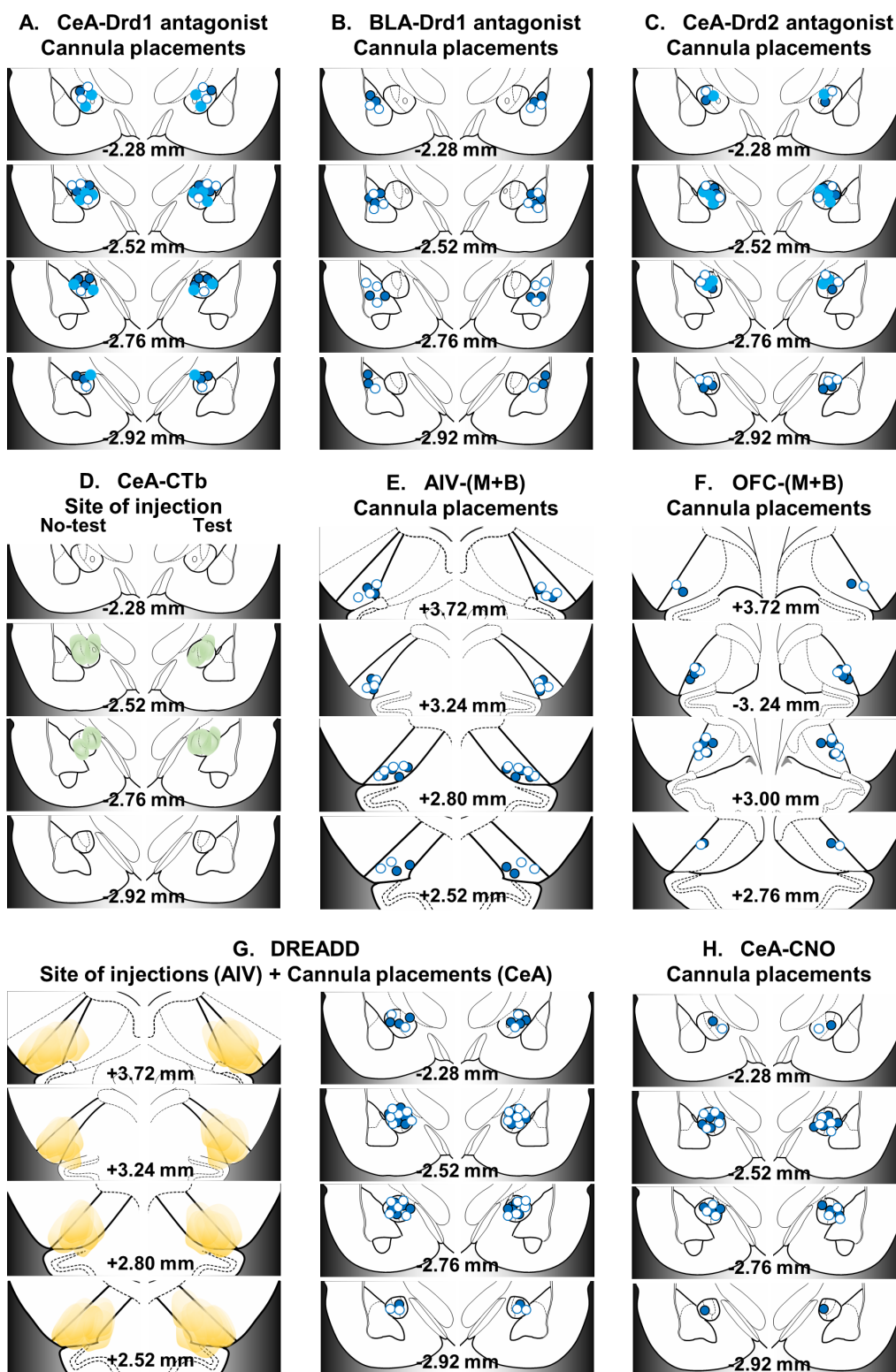


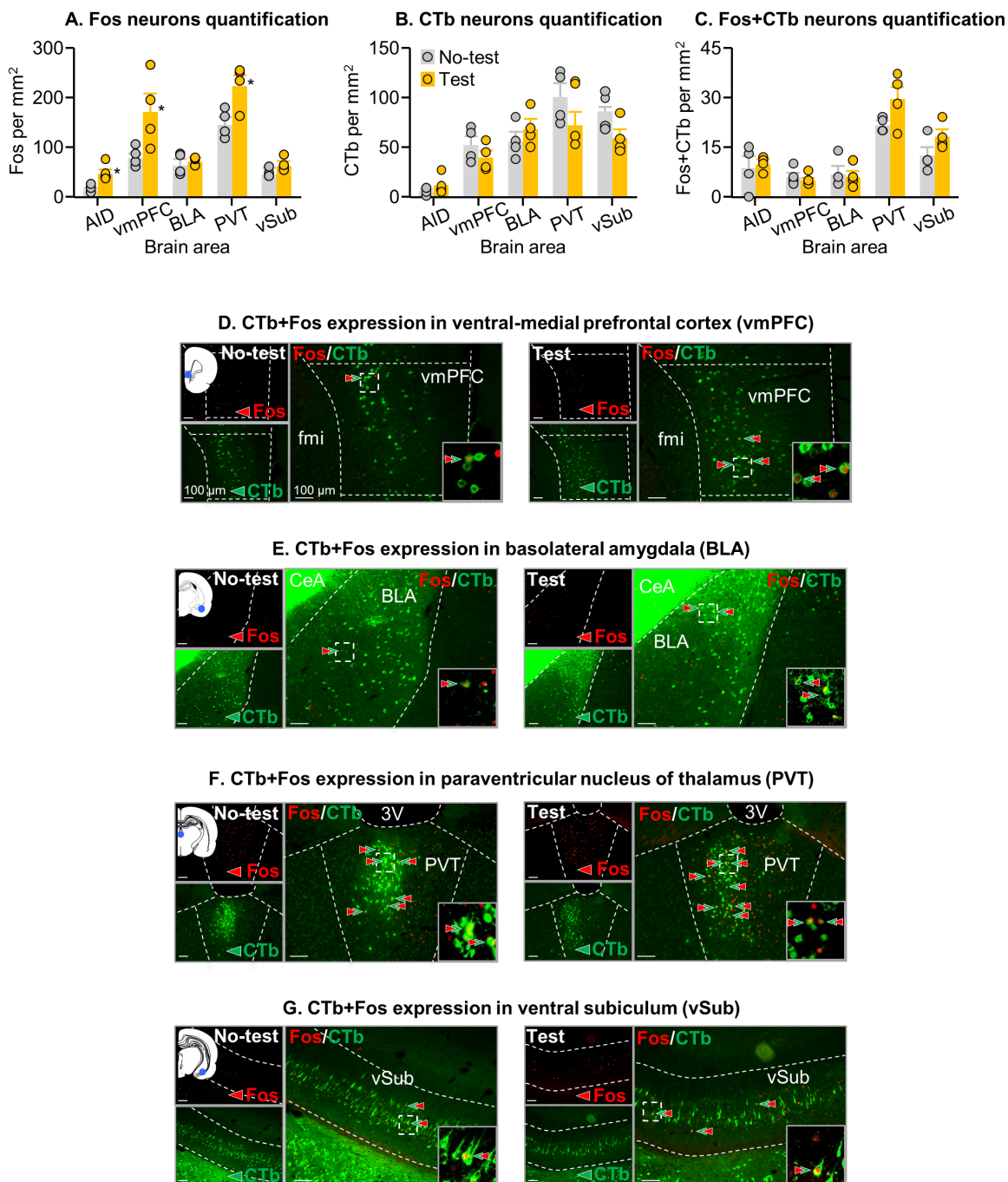
**Figure S1 (Related to Figure 1, Figure 2 and Figure 3). *Effect of Drd1 antagonist and GABA<sub>A</sub> + GABA<sub>B</sub> agonist on food self-administration.*** (A-B) Mean±SEM number of presses on the active and inactive levers during the 1-h test sessions after systemic or CeA SCH39166 injections (n=5-8 per group). (C) Mean±SEM number of lever presses during the 1-h test sessions of M+B injections into the AIV (n=8 per group).



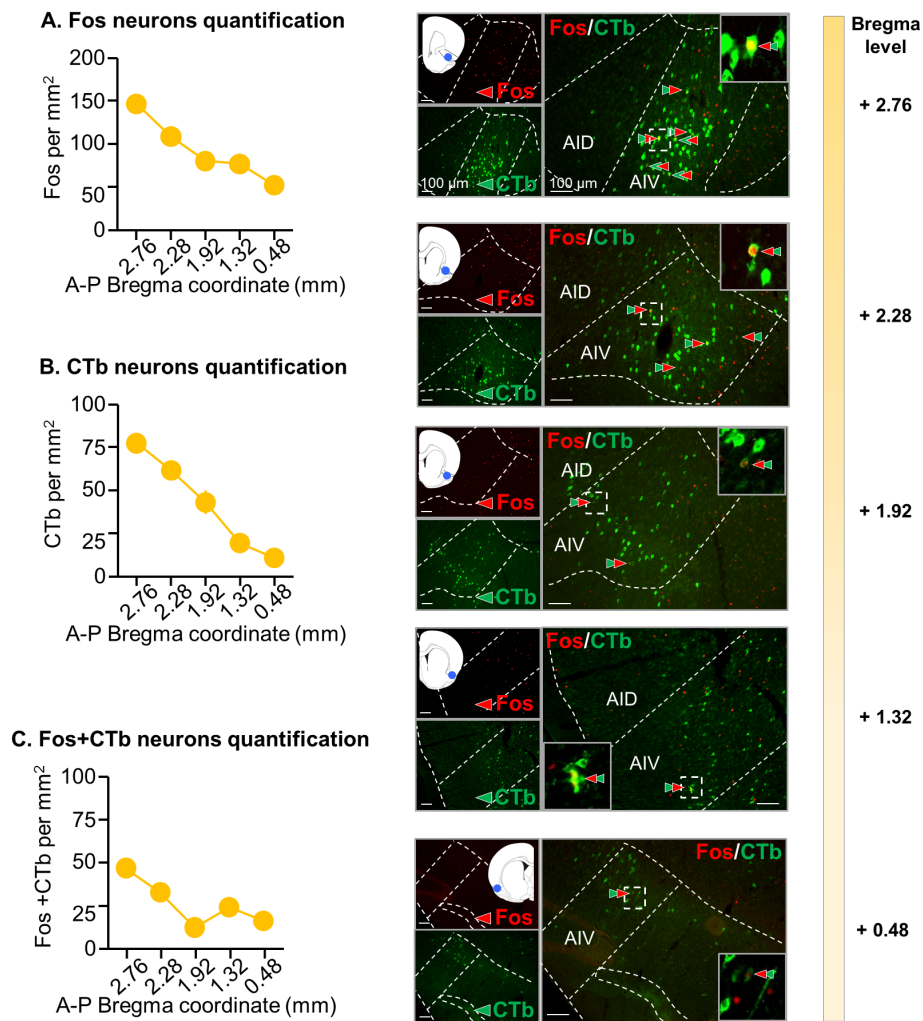
**Figure S2 (Related to Figure 1). Effect of systemic *Drd1* antagonist injections on Fos expression and RNA scope in the CeL and CeM.** (A) Fos immunohistochemistry: Representative photomicrographs of Fos cells in lateral central (CeL) and medial central (CeM) amygdala. (B) Amygdala c-Fos expression: Number of Fos-IR nuclei per mm<sup>2</sup> in the CeL and CeM. \* Different from the other conditions, p<0.05 (C). RNAscope *in situ* hybridization: Representative photomicrographs of CeL and CeM and Fos labelling in the Relapse test and No-test groups, and *Drd1* or *Drd2* labelling in the Relapse test group (*Fos*, white; *Drd1*, green; *Drd2*, red; DAPI, blue). Arrows indicate representative cells. (D) Fos-IR neurons: Number of Fos-IR nuclei per mm<sup>2</sup> in CeL and CeM. \* Different from the No-test group, p<0.05 (E) *Drd1* and *Drd2* positive cells: Number of *Drd1* and *Drd2* cells in CeL and CeM. (F) Fos-IR co-expression with *Drd1* or *Drd2*: Number of double-labeled neurons per mm<sup>2</sup> in the CeL and CeM. \* Different from *Fos+Drd2*, p<0.05. All the data are mean±SEM.



**Figure S3 (Related to Figure 2, Figure 3 and Figure 4). Cannula placements of the injector tips, representative plots of the spread of CTb and hM4Di injections (mm from Bregma) for (A) Drd1 antagonist SCH39166 injection in CeA (white circles = vehicle, **light blue** = 0.5 µg/side and **dark blue** = 1.0 µg/side); (B) Drd1 antagonist SCH39166 injection in BLA (white circles = vehicle and **dark blue** = 1.0 µg/side); (C) Drd2 antagonist raclopride injection in CeA (white circles = vehicle, **light blue** = 0.5 µg/side and **dark blue** = 1.0 µg/side); (D) CTb injection in CeA; (E) Muscimol+Baclofen injection in AIV (white circles = vehicle and **dark blue** = 50 ng+50 ng/side); (F) Muscimol+Baclofen injection in OFC (white circles = vehicle and **dark blue** = 50 ng+50 ng/side); (G) hM4Di injection in AIV (0.75 µg/side **yellow**), and CNO injection in CeA (white circles = vehicle and **dark blue** = 1.0 mM/side); (H) CNO injection in CeA (white circles = vehicle and **dark blue** = 1.0 mM/side). For CTb and hM4Di injection, each injection is plotted at 50% opacity so that overlap of injection sites is apparent with increased color intensity.**



**Figure S4 (Related to Figure 3). Fos and CTb expression from afferent projections AID, vmPFC, BLA, PVT, and vSub to CeA. (A) Number of Fos-IR nuclei per mm<sup>2</sup> for the Relapse test or No-test groups (n=4 per group). (B) Number of CTb-IR nuclei per mm<sup>2</sup>. (C) Number of double-labeled Fos+CTb neurons per mm<sup>2</sup>. Representative photomicrographs (scale=100  $\mu$ m) of Fos and CTb expression in vmPFC (D), BLA (E), PVT (F), and vSub (G) are shown below, **Green arrows**=CTb-IR neurons, **Red arrows**=Fos-IR neurons, **Green+Red arrows**=double-labeled neurons. Data are mean $\pm$ SEM. \* Different from the No-test group, p<0.05.**



**Figure S5 (Related to Figure 3). *Fos* and *CTb* expression at different bregma levels in AIV.** Number of Fos-IR (A), CTb-IR (B), and CTb+Fos-IR double-labeled (C) neurons per mm<sup>2</sup>. Representative photomicrographs (scale=100  $\mu$ m) of Fos and CTb expression at different Bregma levels of AIC (for the Relapse test condition) are shown in the middle. **Green arrows**=CTb-IR neurons, **Red arrows**=Fos-IR neurons, **Green+Red arrows**=double-labeled neurons. Schematic drawing of CTb expression in AI is shown on the left: We normalized the mean data obtained from the total CTb-IR counting at different Bregma levels, adapted from Paxinos and Watson (2008). We assigned 1 to the highest values (**dark yellow**) and 0 to the lowest value (**light yellow/white**). Data are mean $\pm$ SEM. \* Different from the No-test group,  $p < 0.05$ .

**Table S1 (Related to Figure 1, 2, 3, 4, 5, 6, S1, S2, S3, S4 and S5). Statistical analysis.**  
 (SPSS GLM repeated-measures module). Partial Eta<sup>2</sup> = proportion of explained variance.

Figure number	Factor name	F-value	p-value	Partial Eta <sup>2</sup>
Figure 1B. Self-administration RM-ANOVA	Session (Food) (within)	F <sub>5,265</sub> =26.1	<0.001*	0.52
	Session (Meth) (within)	F <sub>14,742</sub> =30.9	<0.001*	0.37
Figure 1C. Choice test RM-ANOVA	Reward (within)	F <sub>1,53</sub> =428.6	<0.001*	0.89
	Session (within)	F <sub>1,53</sub> =1.3	0.27	0.02
	Reward X Session interaction	F <sub>1,53</sub> =31.6	<0.001*	0.37
Figure 1D. Voluntary abstinence RM-ANOVA	Reward (within)	F <sub>1,53</sub> =19020.1	<0.001*	1.00
	Session (within)	F <sub>13,689</sub> =1.6	0.09	0.03
	Reward X Session interaction	F <sub>13,689</sub> =7.4	<0.001*	0.12
Figure 1E. Relapse test Mixed ANOVA	SCH39166 dose (between)	F <sub>1,25</sub> =13.5	0.001*	0.35
	Lever (within)	F <sub>1,25</sub> =83.5	<0.001*	0.77
	Dose X lever interaction	F <sub>1,25</sub> =13.5	0.001*	0.35
Figure 1G. Fos neuron counting Mixed ANOVA	Test (between)	F <sub>1,39</sub> =7.5	0.009*	0.16
	SCH39166 dose (between)	F <sub>1,39</sub> =8.0	0.007*	0.17
	Amygdala sub-region (within)	F <sub>1,39</sub> =50.4	<0.001*	0.56
	Test X SCH39166 dose interaction	F <sub>1,39</sub> =6.3	0.02*	0.14
	Test X Amygdala sub-region interaction	F <sub>1,39</sub> =10.7	0.002*	0.22
	SCH39166 dose X Amygdala sub-region interaction	F <sub>1,39</sub> =14.3	0.001*	0.27
	Test X SCH39166 dose X Amygdala sub-region interaction	F <sub>1,39</sub> =7.0	0.01*	0.15
Figure 1H. Relapse test for RNAscope RM-ANOVA	Lever (within)	F <sub>1,5</sub> =45.2	<0.001*	0.90
Figure 1J. Fos neurons counting Mixed ANOVA	Test (between)	F <sub>1,8</sub> =13.7	0.006*	0.63
	Amygdala sub-region (within)	F <sub>1,8</sub> =23.8	0.001*	0.75
	Extinction test X Amygdala sub-region interaction	F <sub>1,8</sub> =14.5	0.005*	0.64
Figure 1K. Drd1 and Drd2 cell counting Mixed ANOVA	Test (between)	F <sub>1,8</sub> =0.0	0.94	0.001
	Amygdala sub-region (within)	F <sub>1,8</sub> =0.3	0.59	0.04
	Cell type (within)	F <sub>1,8</sub> =33.0	<0.001*	0.81
	Test X Amygdala sub-region interaction	F <sub>1,8</sub> =0.0	0.86	0.004
	Test X Cell type interaction	F <sub>1,8</sub> =0.0	0.85	0.005
	Test X Amygdala sub-region X Cell type interaction	F <sub>1,8</sub> =0.0	0.95	0.001
	Amygdala sub-region X Cell type interaction	F <sub>1,8</sub> =38.5	<0.001*	0.83
Figure 1L. Double labeled cells counting Mixed ANOVA	Test (between)	F <sub>1,8</sub> =8.9	0.02*	0.87
	Amygdala sub-region (within)	F <sub>1,8</sub> =38.6	<0.001*	0.83
	Cell type (within)	F <sub>1,8</sub> =16.1	0.004*	0.67
	Test X Amygdala sub-region interaction	F <sub>1,8</sub> =8.0	0.02	0.50
	Test X Cell type interaction	F <sub>1,8</sub> =7.8	0.02	0.49
	Test X Amygdala sub-region X Cell type interaction	F <sub>1,8</sub> =3.4	0.10	0.30
	Amygdala sub-region X Cell type interaction	F <sub>1,8</sub> =0.1	0.82	0.01
Figure 2B. Self-administration RM-ANOVA	Session (Food) (within)	F <sub>5,300</sub> =45.5	<0.001*	0.43
	Session (Meth) (within)	F <sub>14,840</sub> =49.7	<0.001*	0.45
Figure 2C. Choice tests RM-ANOVA	Reward (within)	F <sub>1,60</sub> =815.0	<0.001*	0.93
	Session (within)	F <sub>1,60</sub> =12.9	<0.001*	0.18
	Reward X session interaction	F <sub>1,60</sub> =6.6	0.01*	0.10
Figure 2D. Voluntary abstinence RM-ANOVA	Reward (within)	F <sub>1,60</sub> =8069.4	<0.001*	0.99
	Session (within)	F <sub>13,780</sub> =0.3	0.99	0.01
	Reward X session interaction	F <sub>13,780</sub> =17.1	<0.001*	0.22
Figure 2E. Relapse test for CeA-Drd1 antagonist injection Mixed ANOVA	SCH39166 dose (between)	F <sub>2,21</sub> =8.4	0.002*	0.44
	Lever (within)	F <sub>1,21</sub> =158.4	<0.001*	0.88
	Dose X lever interaction	F <sub>2,21</sub> =8.2	0.002*	0.44
Figure 2F. Relapse test for BLA-Drd1 antagonist injection Mixed ANOVA	SCH39166 dose (between)	F <sub>1,16</sub> =0.0	0.94	0.00
	Lever (within)	F <sub>1,16</sub> =110.9	<0.001*	0.87
	Dose X lever interaction	F <sub>1,16</sub> =0.0	0.98	0.00

Figure 2G. Relapse test for CeA-Drd2 antagonist injection Mixed-ANOVA	Raclopride dose (between) Lever (within) Dose X lever interaction	$F_{2,16}=0.0$ $F_{1,16}=387.3$ $F_{2,16}=0.1$	0.99 <0.001* 0.91	0.002 0.71 0.01
Figure 3B. Self-administration RM-ANOVA	Session (Food) (within) Session (Meth) (within)	$F_{5,225}=34.8$ $F_{14,630}=32.6$	<0.001* <0.001*	0.44 0.42
Figure 3C. Choice test RM-ANOVA	Reward (within) Session (within) Reward X session interaction	$F_{1,45}=172.7$ $F_{1,45}=3.1$ $F_{1,45}=5.9$	<0.001* 0.08 0.02*	0.79 0.07 0.12
Figure 3D. Voluntary abstinence RM-ANOVA	Reward (within) Session (within) Reward X session interaction	$F_{1,45}=793.0$ $F_{13,585}=20.6$ $F_{13,585}=6.6$	<0.001* <0.001* <0.001*	0.95 0.31 0.13
Figure 3E. Relapse test CeA-CTb Friedman Test	Lever (within)	$\chi^2(1)=4.0$	0.046*	
Figure 3F. Fos, CTb, and Fos+CTb neurons counting AIV (also see S4) Mann-Whitney	Test (between) Fos CTb Fos+CTb	$U=0.0$ $U=4.0$ $U=0.0$	0.02* 0.25 0.02*	
Figure 3G. Relapse test for AIV-M+B injection Mixed-ANOVA	M+B dose (between) Lever (within) Dose X lever interaction	$F_{1,20}=9.1$ $F_{1,20}=102.1$ $F_{1,20}=13.0$	0.007* <0.001* 0.002*	0.31 0.84 0.39
Figure 3H. Relapse test for OFC-M+B injection Mixed-ANOVA	M+B dose (between) Lever (within) Dose X lever interaction	$F_{1,14}=0.1$ $F_{1,14}=24.8$ $F_{1,14}=0.3$	0.77 <0.001* 0.60	0.01 0.64 0.02
Figure 4B. Self-administration RM-ANOVA	Session (Food) (within) Session (Meth) (within)	$F_{5,235}=18.7$ $F_{14,658}=22.0$	<0.001* <0.001*	0.28 0.32
Figure 4C. Choice test RM-ANOVA	Reward (within) Session (within) Reward X session interaction	$F_{1,47}=198.8$ $F_{1,47}=0.8$ $F_{1,47}=17.4$	<0.001* 0.39 <0.001*	0.81 0.01 0.27
Figure 4D. Voluntary abstinence RM-ANOVA	Reward (within) Session (within) Reward X session interaction	$F_{1,47}=968.1$ $F_{13,611}=1.4$ $F_{13,611}=9.5$	<0.001* 0.14 <0.001*	0.95 0.03 0.17
Figure 4E Left. Relapse test AIV-DREADD/CeA-CNO Mixed ANOVA	CNO dose (between) Lever (within) Dose X lever interaction	$F_{1,28}=7.3$ $F_{1,28}=127.3$ $F_{1,28}=7.5$	0.01* <0.001* 0.01*	0.21 0.82 0.21
Figure 4E Right. Fos neurons counting in CeA with CeA-CNO One-way ANOVA	CNO dose (between)	$F_{1,28}=28.4$	0.001*	0.75
Figure 4F Left. Relapse test CeA-CNO injection Mixed ANOVA	CNO dose (between) Lever (within) Dose X lever interaction	$F_{1,15}=0.0$ $F_{1,15}=159.9$ $F_{1,15}=0.3$	0.89 <0.001* 0.62	0.001 0.91 0.02
Figure 4F Right. Fos neurons counting in CeA with CeA-CNO One-way ANOVA	CNO dose (between)	$F_{1,15}=0.0$	0.91	0.001
Figure 5A. Inhibition of AIV terminals in CeA with CNO: evoked EPSC amplitude Mixed-ANOVA	mCherry expression (between) CNO dose (within) CNO dose X mCherry expression interaction	$F_{1,14}=0.02$ $F_{1,14}=4.6$ $F_{1,14}=6.7$	0.9 0.05 0.02*	0.001 0.25 0.32
Figure 5B Left. Spontaneous EPSC frequency Mixed-ANOVA	mCherry expression (between) CNO dose (within) CNO dose X mCherry expression interaction	$F_{1,14}=0.05$ $F_{1,14}=5.3$ $F_{1,14}=9.6$	0.82 0.04* 0.008*	0.004 0.28 0.41
Figure 5B Middle. Spontaneous EPSC amplitude Mixed-ANOVA	mCherry expression (between) CNO dose (within) CNO dose X mCherry expression interaction	$F_{1,14}=0.06$ $F_{1,14}=0.26$ $F_{1,14}=0.03$	0.81 0.62 0.86	0.004 0.02 0.002



Figure 6A. vGluT1+mCherry quantification Friedman Test	Amygdala sub-region (within)	$\chi^2(1)=3.0$	0.08	
Figure 6B. TTX effect on light-evoked EPSCs in CeA RM-ANOVA	Baseline before TTX vs. after TTX (within)	$F_{1,8}=0.4$	0.53	0.05
Figure S1A. Systemic Drd1 antagonist Mixed-ANOVA	SCH39166 dose (between) Lever (within) SCH39166 dose x Lever interaction	$F_{4,20}=3.3$ $F_{1,20}=133.2$ $F_{4,20}=3.7$	0.03* <0.001* 0.02*	0.40 0.87 0.43
Figure S1B. CeA-Drd1 antagonist Mixed-ANOVA	SCH39166 dose (between) Lever (within) SCH39166 dose x Lever interaction	$F_{2,19}=0.9$ $F_{1,19}=155.3$ $F_{2,19}=1.0$	0.42 <0.001* 0.37	0.09 0.89 0.10
Figure S1C. AIV-M+B Mixed-ANOVA	M+B dose (between) Lever (within) M+B dose x Lever interaction	$F_{1,14}=0.3$ $F_{1,14}=41.5$ $F_{1,14}=0.3$	0.62 <0.001* 0.60	0.02 0.75 0.02
Figure S2B. Fos neuron counting Mixed-ANOVA	Test (between) Dose (between) CeA sub-region (within) Test x Dose interaction Test x CeA sub-region interaction Dose x CeA sub-region interaction Test x Dose x CeA sub-region interaction	$F_{1,39}=64.0$ $F_{1,39}=23.4$ $F_{1,39}=4.2$ $F_{1,39}=34.2$ $F_{1,39}=0.1$ $F_{1,39}=1.2$ $F_{1,39}=0.1$	<0.001* <0.001* 0.046* <0.001* 0.77 0.28 0.77	0.62 0.38 0.10 0.47 0.002 0.03 0.002
Figure S2D. Fos neuron counting Mixed-ANOVA	Test (between) CeA sub-region (within) Test x CeA sub-region interaction	$F_{1,8}=23.4$ $F_{1,8}=0.1$ $F_{1,8}=0.2$	0.001* 0.82 0.66	0.75 0.007 0.03
Figure S2E. Drd1 and Drd2 cell counting Mixed-ANOVA	Test (between) CeA sub-region (within) Cell type (within) Test x CeA sub-region interaction Test x Cell type interaction CeA sub-region x Cell type interaction Test x CeA sub-region x Cell type interaction	$F_{1,8}=0.1$ $F_{1,8}=2.7$ $F_{1,8}=0.3$ $F_{1,8}=0.5$ $F_{1,8}=0.03$ $F_{1,8}=1.7$ $F_{1,8}=0.1$	0.73 0.14 0.61 0.49 0.87 0.23 0.81	0.02 0.25 0.03 0.06 0.004 0.18 0.007
Figure S2F. Double-labeled cells counting Mixed-ANOVA	Test (between) CeA sub-region (within) Cell type (within) Test x CeA sub-region interaction Test x Cell type interaction CeA sub-region x Cell type interaction Test x CeA sub-region x Cell type interaction	$F_{1,8}=22.4$ $F_{1,8}=0.2$ $F_{1,8}=75.9$ $F_{1,8}=0.2$ $F_{1,8}=30.7$ $F_{1,8}=0.5$ $F_{1,8}=0.5$	0.001* 0.70 <0.001* 0.70 0.001* 0.51 0.51	0.74 0.02 0.91 0.02 0.79 0.06 0.06
Figure S3A. Fos neuron counting Mann-Whitney Test	Test (between) vmPFC AID BLA PVT vSub	$U=1.0$ $U=0.0$ $U=8.0$ $U=1.0$ $U=1.5$	0.04* 0.02* 1.0 0.04* 0.06	
Figure S3B. CTb neuron counting Mann-Whitney Test	Test (between) vmPFC AID BLA PVT vSub	$U=4.0$ $U=4.5$ $U=4.5$ $U=2.0$ $U=2.0$	0.25 0.31 0.08 0.08 0.08	
Figure S3C. Fos+CTb neuron counting Mann-Whitney Test	Test (between) vmPFC AID BLA PVT vSub	$U=6.5$ $U=7.5$ $U=7.5$ $U=4.0$ $U=3.0$	0.66 0.89 0.88 0.25 0.15	
Figure S4A. Fos neuron counting Friedman Test	Bregma coordinate (within)	$\chi^2(4)=15.4$	0.004*	
Figure S4B. CTb neuron counting Friedman Test	Bregma coordinate (within)	$\chi^2(4)=16.0$	0.003*	
Figure S4C. Fos+CTb neuron counting Friedman Test	Bregma coordinate (within)	$\chi^2(4)=14.7$	0.01*	