Supplemental Materials

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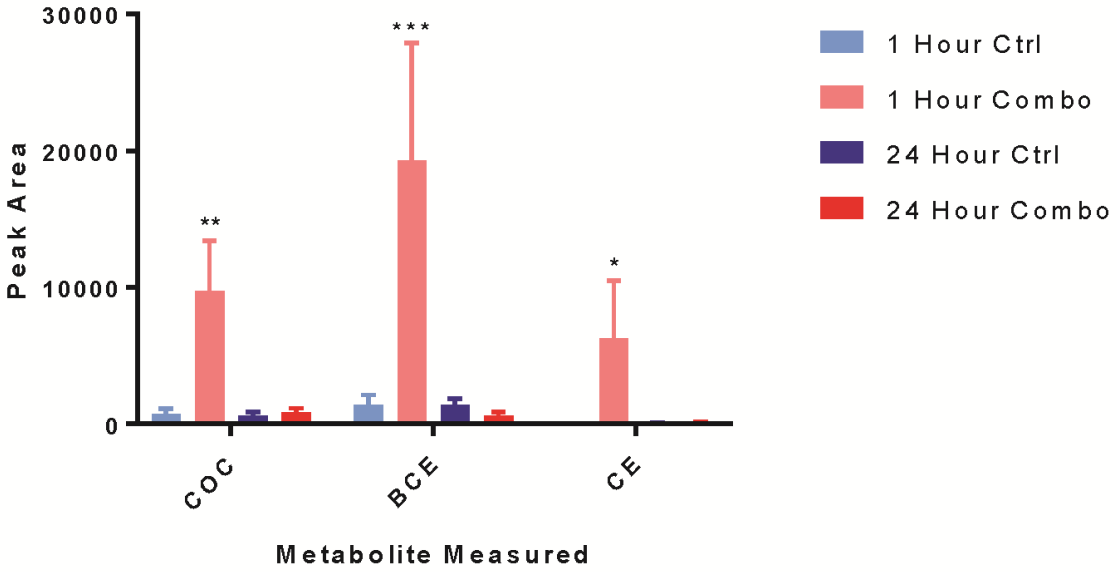
Supplemental Methods

Analysis of Cocaine & Metabolites Using LC-MS

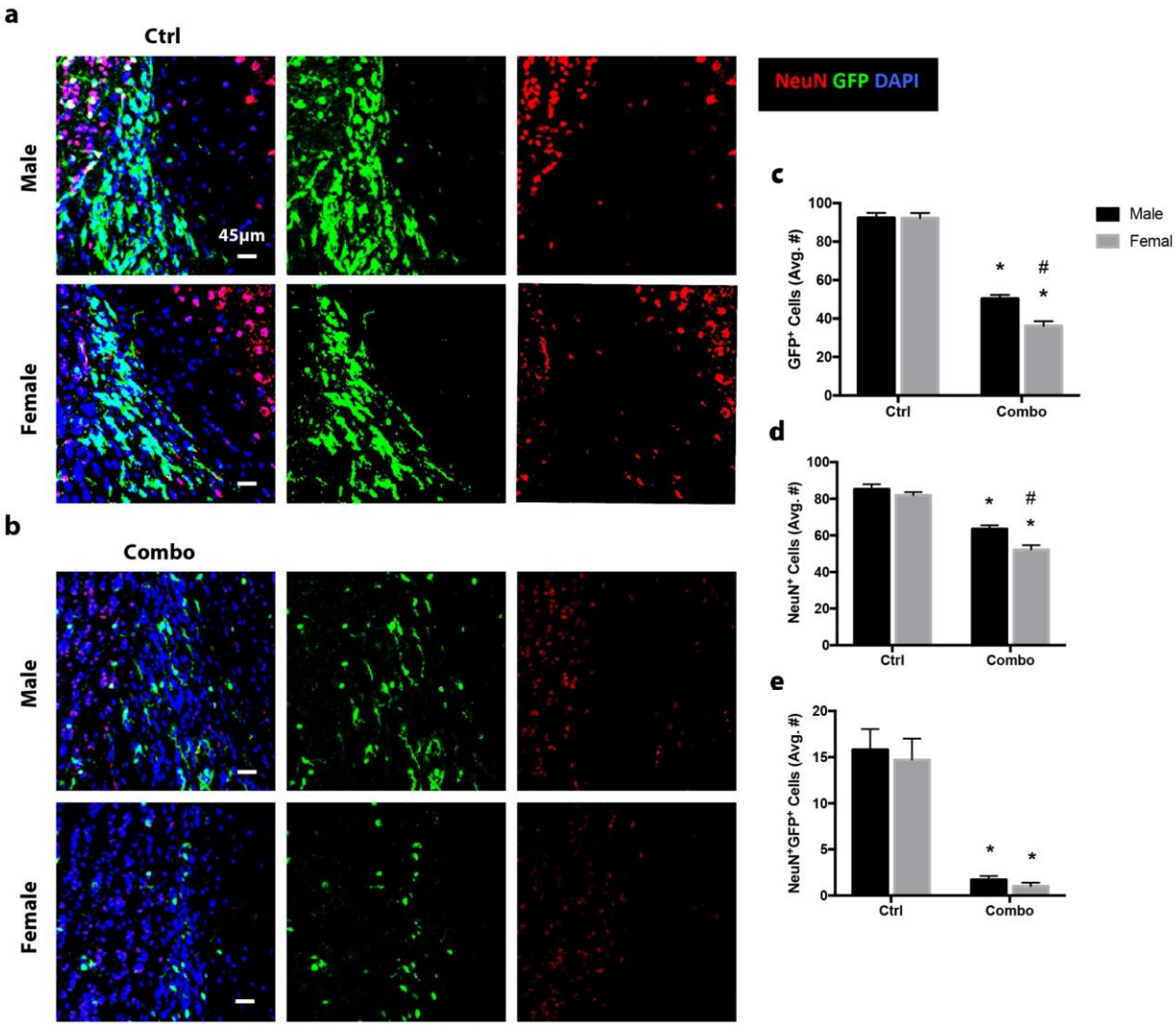
An Agilent 1260 HPLC system with a binary gradient pump, autosampler and column oven (50°C) was used for the chromatographic separation. An Agilent SB-C18 1.8uM 2.1 X 50mm column was used. Mobile phase A was water + 0.1% formic acid and mobile phase B acetonitrile + 0.1% formic acid. A flow rate 500 µL/min was used. The gradient with a total run time of 12 minutes 0-1min 98% A, 1-7min a linear gradient to 35% A, 7-7.1 min to 2% A, 7.1-9min 2% A, 9-9.1 min 98% A, 9.1-12min 98% A. The injection volume was set to 10 µL.

A SCIEX QTRAP 6500 system with Turbo V source with ESI probe was used. The target compounds were detected in positive polarity. The ion source parameters were optimized for the new LC conditions using the Compound Optimization (FIA) function in Analyst® software and are as follows: Curtain gas (40), CAD set to high, Ionspray voltage 4500, Temperature 50C, GS1 50, GS2 50, DP ranged from 76-81 volts, CE ranged from 27-41 volts, CXP ranged from 10-16 volts. Two characteristic MRM transitions were monitored for each analyte, and 1 MRM transition for each internal standard.

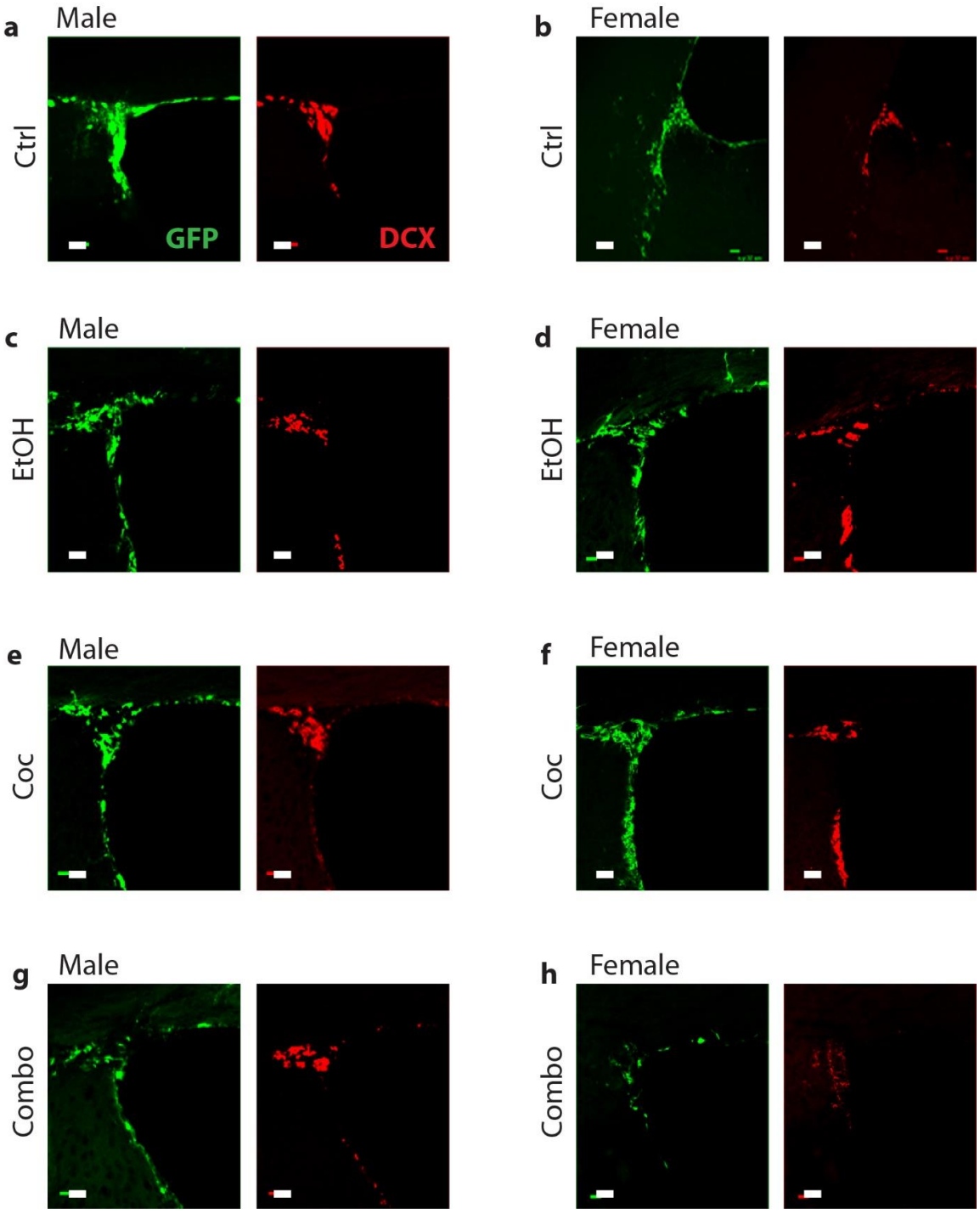
Supplemental Figures and Figure Legends



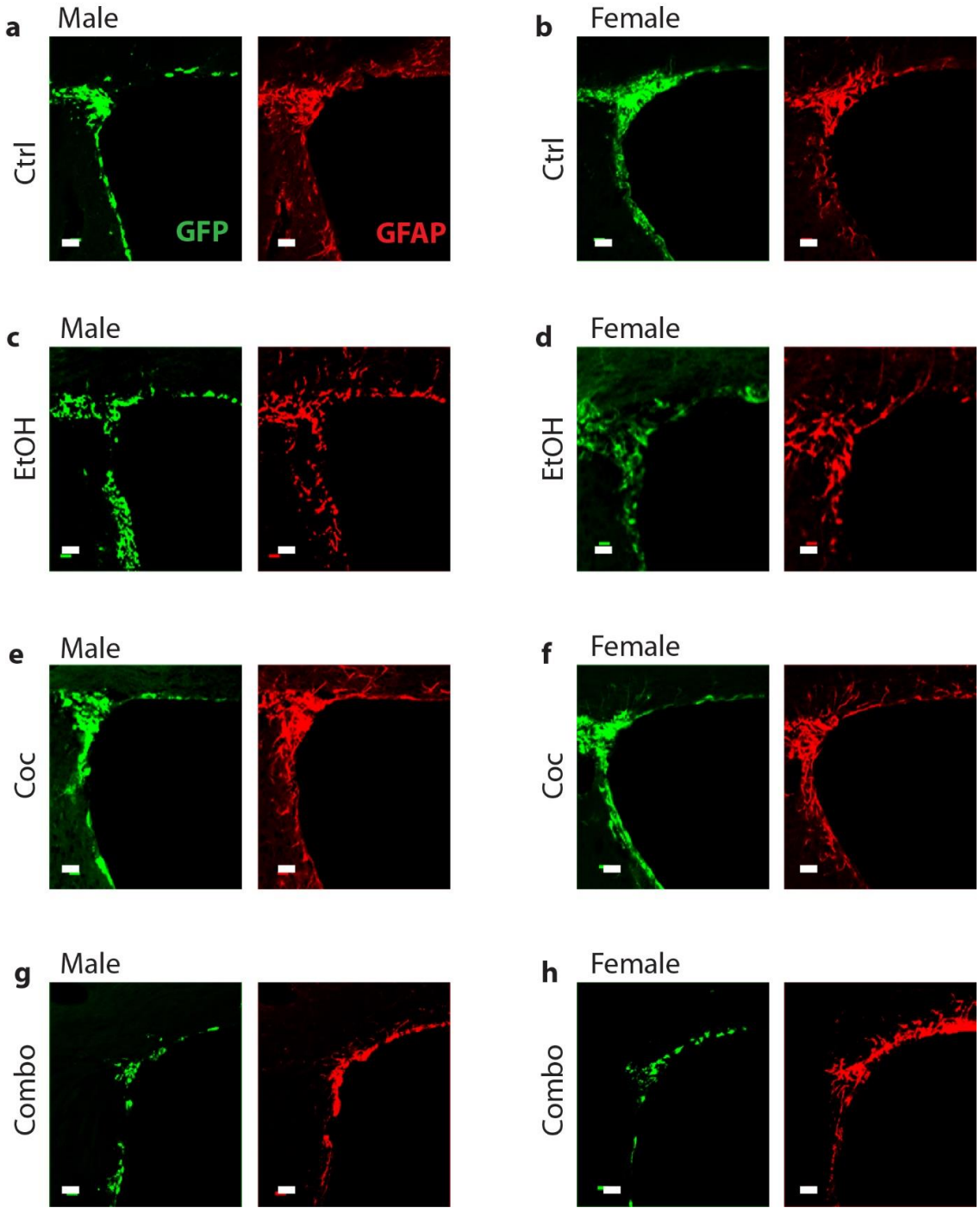
Supplementary Figure 1. Analyses of cocaine and metabolite concentrations in blood using LC-MS. Related to Figure 1. Chart showing the cocaine (Coc), benzoylecgonine (BCE), and cocaethylene (CE) analyses of animals from control (Ctrl) and treatment with ethanol and cocaine (Combo), n=5, at 1 or 24 hour intervals following cocaine administration.



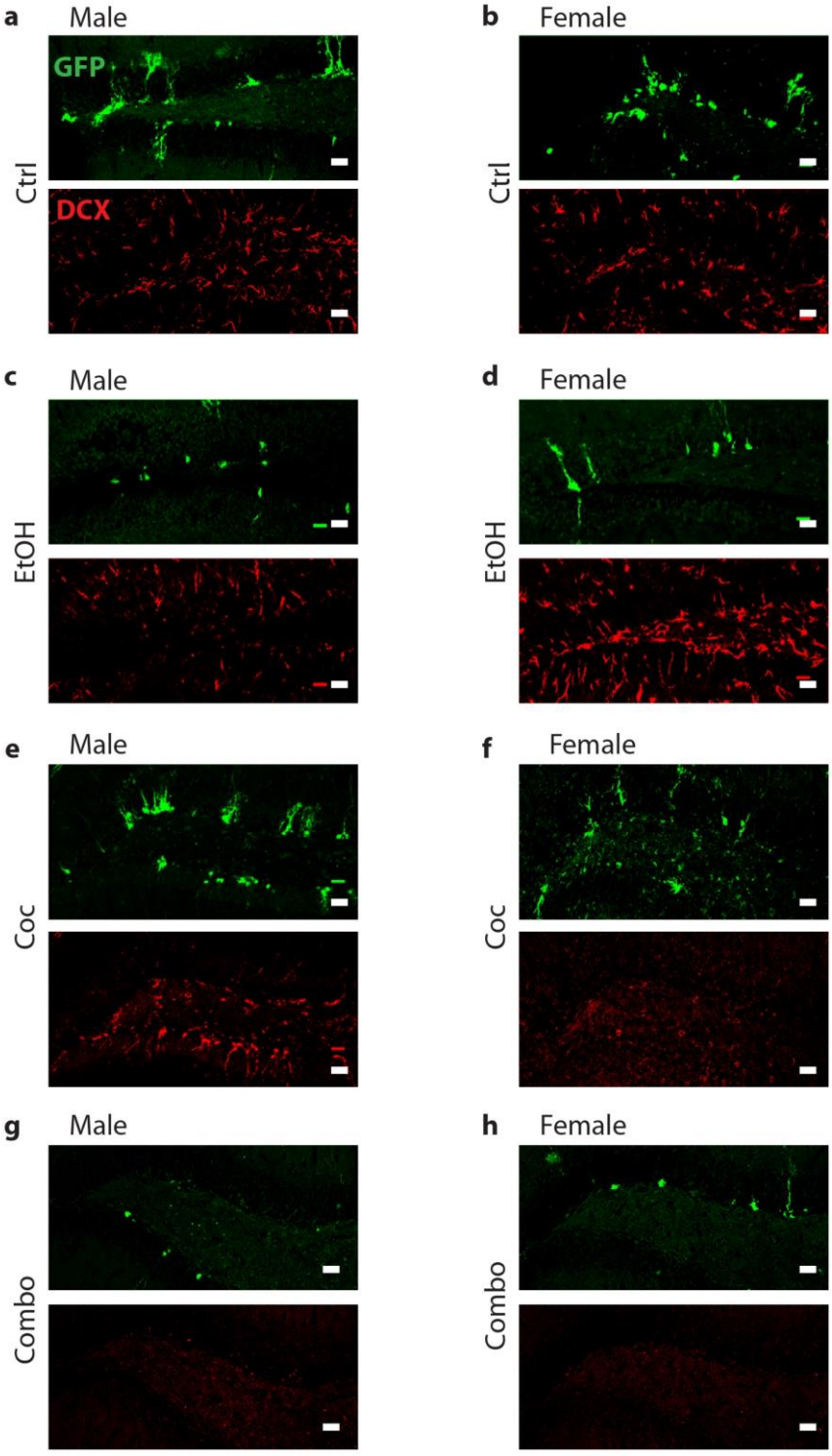
Supplementary Figure 2. Reduction of neurogenesis in the olfactory bulb. Related to Figure 2. (**a**) Representative images of control male and female mice stained with stem cell marker (GFP green), neuronal marker (NeuN red), and merged with nuclear maker DAPI (blue). (**b**) Representative images of combination drug-treated (Combo) male and female mice. (**c-e**) Quantification of GFP^+, $NeuN^+$, and $NeuN^+GFP^+$ cells in the olfactory bulb. Values are shown as mean ±SEM, *$p<0.05$ compared to control, $^{\#}p<0.05$ compared to other sex in the same group, n=3 mice per sex per group. Scale bars, 45μm.



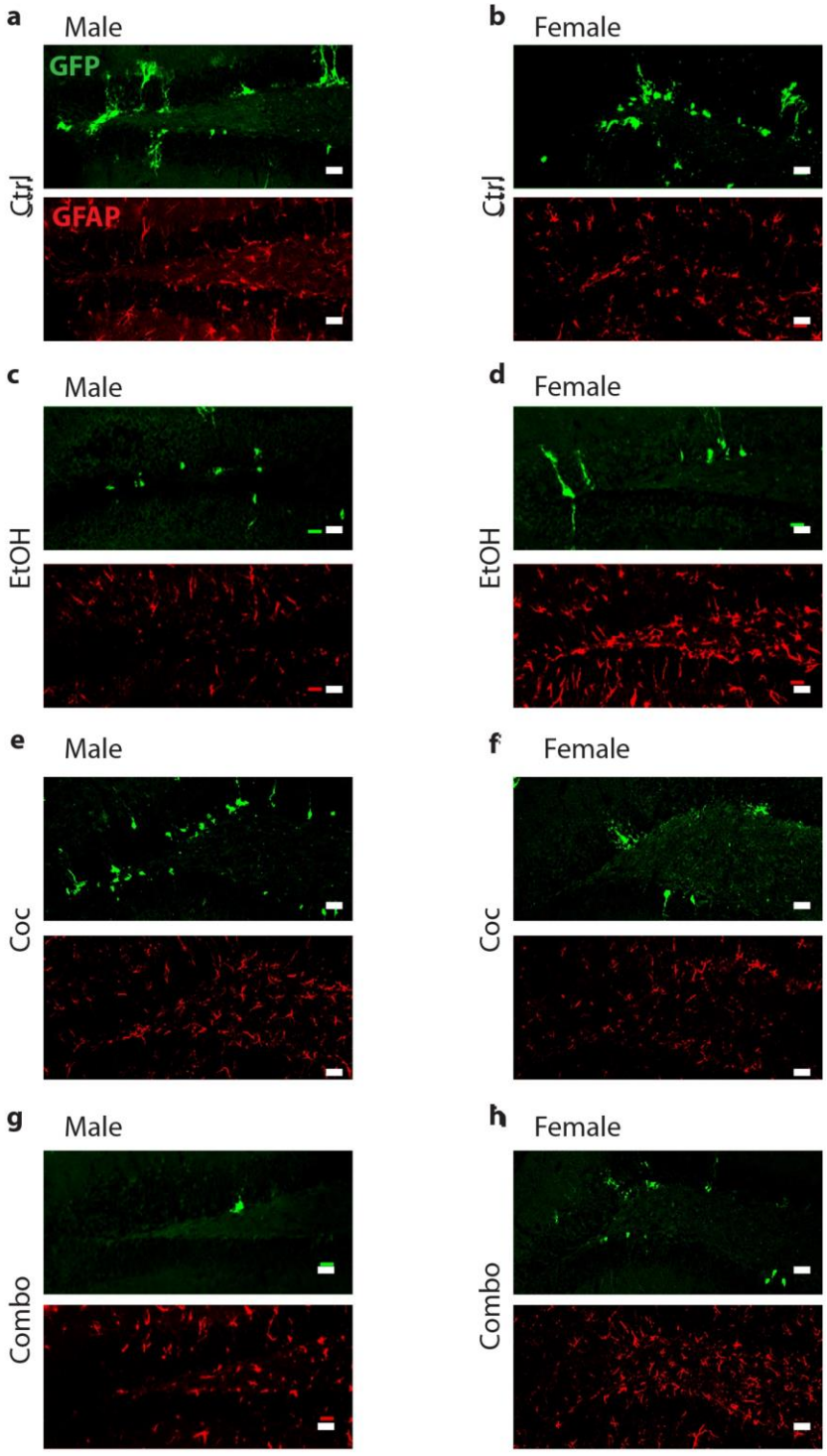
Supplementary Figure 3. Individual channels of SVZ immunohistochemical stains. Related to Figure 2. (**a-b**) Single channel of representative images of control male and female mice stained with stem cell marker (GFP green), neuronal marker (DCX red). (**c-d**) Ethanol-treated (EtOH) male and female mice. (**e-f**) Cocaine-treated (Coc) male and female mice. (**g-h**) Combination treatment of (Combo) male and female mice. Scale bars, 45μm.



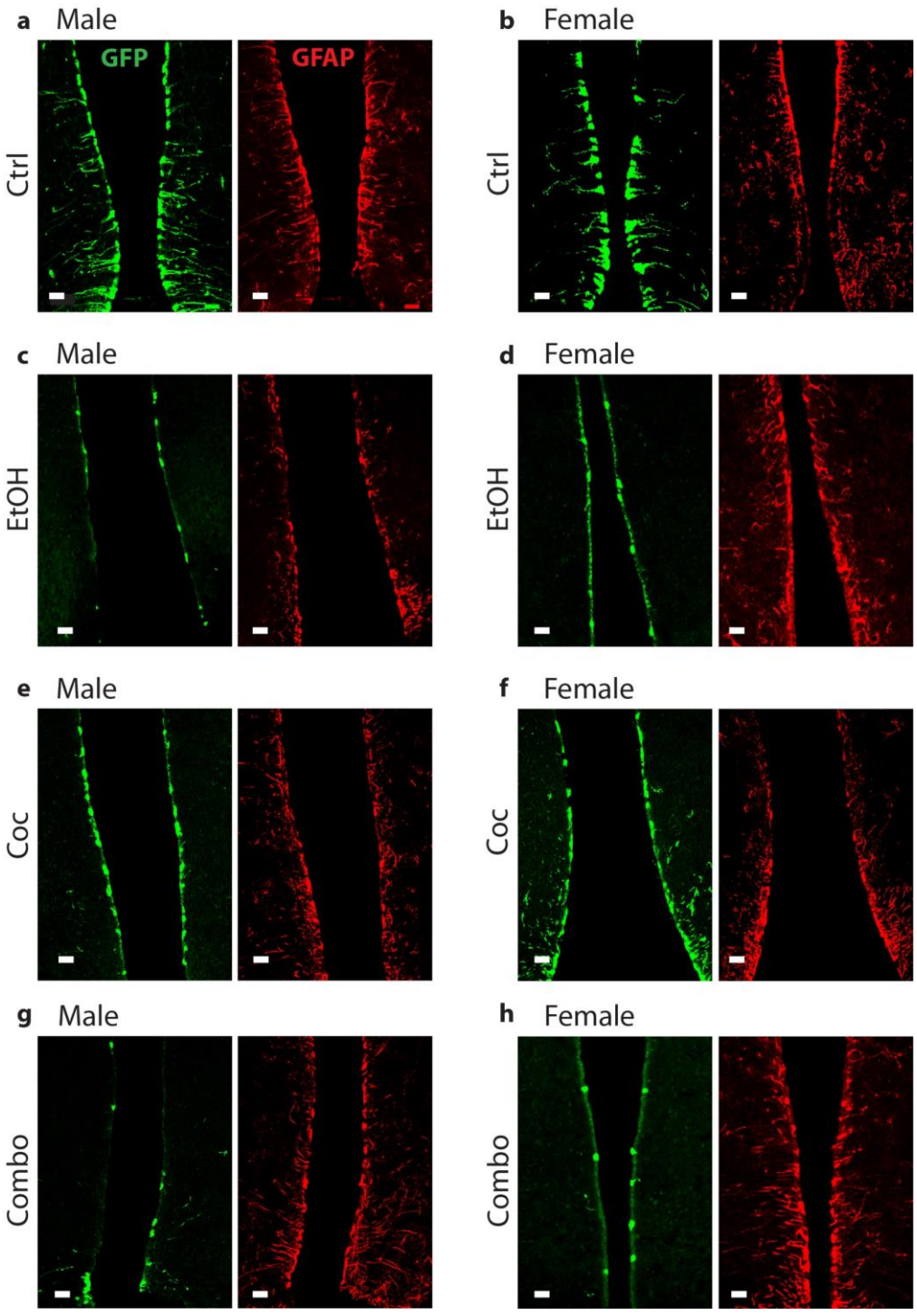
Supplementary Figure 4. Individual channels of SVZ immunohistochemical stains. Related to Figure 3. (**a-b**) Single channel of representative images of control male and female mice stained with stem cell marker (GFP green), astroglial markers (GFAP red). (**c-d**) Ethanol-treated (EtOH) male and female mice. (**e-f**) Cocaine-treated (Coc) male and female mice. (**g-h**) Combination treatment of (Combo) male and female mice. Scale bars, 45μm.



Supplementary Figure 5. Individual channels of SGZ immunohistochemical stains. Related to Figure 4. (**a-b**) Single channel of representative images of control male and female mice stained with stem cell marker (GFP green), neuronal marker (DCX red). (**c-d**) Ethanol-treated (EtOH) male and female mice. (**e-f**) Cocaine-treated (Coc) male and female mice. (**g-h**) Combination treatment of (Combo) male and female mice. Scale bars, 45μm.



Supplementary Figure 6. Individual channels of SGZ immunohistochemical stains. Related to Figure 5. (**a-b**) Single channel of representative images of control male and female mice stained with stem cell marker (GFP green), astroglial markers (GFAP red). (**c-d**) Ethanol-treated (EtOH) male and female mice. (**e-f**) Cocaine-treated (Coc) male and female mice. (**g-h**) Combination treatment of (Combo) male and female mice. Scale bars, 45μm.



Supplementary Figure 7. Individual channels of TL immunohistochemical stains. Related to Figure 6. (**a-b**) Single channel of representative images of control male and female mice stained with stem cell marker (GFP green), astroglial markers (GFAP red). (**c-d**) Ethanol-treated (EtOH) male and female mice. (**e-f**) Cocaine-treated (Coc) male and female mice. (**g-h**) Combination treatment of (Combo) male and female mice. Scale bars, 45μm.