Supplemental Table S2. Full ANOVA outcomes.

Table S2A. ANOVA outcomes for cocaine dose-response functions, repeated VU0152099 dosing

	Cocaine dose	Treatment day	Interaction
% cocaine choice Baseline vs.	$F_{(1.9,13.6)}=46.5$, $p<0.0001$	$F_{(2.3,16.3)}=4.1$, $p=0.03$	$F_{(3.3,20.2)}=1.7$, $p=0.19$
Day 1	$F_{(1.3,9.3)}=14.8$, $p=0.003$	$F_{(1,7)}=1.7$, $p=0.24$	$F_{(1.5,10.8)}=2.8$, $p=0.11$
Day 4	$F_{(1.8,12.8)}=21.7$, $p<0.0001$	$F_{(1,7)}=0.59$, $p=0.47$	$F_{(1.9,13.4)}=0.92$, $p=0.42$
Day 5	$F_{(2.1,14.4)}=35.9$, $p<0.0001$	$F_{(1,7)}=4.6$, $p=0.069$	$F_{(1.9,13.6)}=1.6$, $p=0.23$
Day 6	$F_{(1.6,11.2)}=13.4$, $p=0.002$	$F_{(1,7)}=7.3$, $p=0.03$	$F_{(1.3,7.6)}=5.1$, $p=0.049$
Day 7	$F_{(2.0,13.9)}=14.0$, $p=0.0005$	$F_{(1,7)}=25.0$, $p=0.002$	$F_{(2.3,10.5)}=10.3$, $p=0.003$
Post day 4	$F_{(2.3,16.7)}=20.3$, $p<0.0001$	$F_{(1,7)}=1.9$, $p=0.21$	$F_{(2.3,13.3)}=2.7$, $p=0.10$
Cocaine reinforcers Baseline vs.	$F_{(1.6,11.3)}=13.8$, $p=0.001$	$F_{(3.3,23.0)}=3.6$, $p=0.02$	$F_{(20,125)}=1.9$, $p=0.01$
Day 1	$F_{(1.5,10.5)}=40.7$, $p<0.0001$	$F_{(1,7)}=2.8$, $p=0.14$	$F_{(1.6,11.2)}=3.7$, $p=0.067$
Day 4	$F_{(1.8,12.7)}=49.8$, $p<0.0001$	$F_{(1,7)}=2.0$, $p=0.21$	$F_{(1.9,13.6)}=1.1$, $p=0.37$
Day 5	$F_{(1.9,13.6)}=95.0$, $p<0.0001$	$F_{(1,7)}=4.8$, $p=0.064$	$F_{(1.8,12.3)}=1.4$, $p=0.27$
Day 6	$F_{(1.7,11.6)}=31.4$, $p<0.0001$	$F_{(1,7)}=3.5$, $p=0.11$	$F_{(2.0,9.8)}=2.3$, $p=0.15$
Day 7	$F_{(2.3,16.4)}=20.3$, $p<0.0001$	$F_{(1,7)}=11.5$, $p=0.02$	$F_{(3.2,14.3)}=9.0$, $p=0.001$
Post day 4	$F_{(2.4,16.6)}=57.3$, $p<0.0001$	$F_{(1,7)}=3.1$, $p=0.12$	$F_{(2.3,12.4)}=1.5$, $p=0.26$
Food reinforcers	$F_{(2.6,18.0)}=50.7$, $p<0.0001$	$F_{(1.5,10.6)}=1.0$, $p=0.37$	$F_{(3.9,24.1)}=2.2$, $p=0.10$
Total response rate	$F_{(1.4,10.0)}=4.6$, $p=0.048$	$F_{(1.6,11.5)}=0.78$, $p=0.46$	$F_{(2.7,17.0)}=1.2$, $p=0.34$
Cocaine+Food levers response rate	$F_{(1.7,12.2)}=2.2$, $p=0.16$	$F_{(1.8,12.3)}=1.3$, $p=0.30$	$F_{(4.5,28.3)}=0.58$, $p=0.70$

Table S2B. ANOVA outcomes for session-wide cocaine and food intakes and cocaine A_{50}

	Mixed-effect analysis	Test for trend
Acute dosing, effect of VU0152099 dose		
Log(A_{50}) cocaine dose	$F_{(1.8,9.3)}=3.9$, $p=0.06$	Nonlinear $F_{(5,32)}=3.8$, $p=0.008$
Cocaine intake / session	$F_{(1.4,7.9)}=3.5$, $p=0.09$	Nonlinear $F_{(5,33)}=3.0$, $p=0.02$
Food intake / session	$F_{(1.6,8.9)}=2.8$, $p=0.12$	Nonlinear $F_{(5,33)}=2.8$, $p=0.03$
Repeated dosing, effect of day		
Log(A_{50}) cocaine dose	$F_{(2.6,14.9)}=3.4$, $p=0.054$	Linear $F_{(1,38)}=11.3$, $p=0.002$
Cocaine intake / session	$F_{(1.4,8.7)}=2.5$, $p=0.15$	Linear $F_{(1,32)}=9.7$, $p=0.004$
Food intake / session	$F_{(1.5,9.5)}=1.0$, $p=0.37$	No significant trend, $p>0.28$

Table S2C. ANOVA outcomes for cocaine dose-response functions, acute VU0152099 dosing

VU0152099 dose	Cocaine unit dose	Treatment day vs. baseline	Cocaine by treatment Interaction
Percent cocaine choice			
Vehicle	$F_{(1.1,6.6)}=47.6$, $p=0.0003$	$F_{(1,6)}=5.7$, $p=0.054$	$F_{(1.3,7.0)}=7.9$, $p=0.02$
0.32 mg/kg	$F_{(1.5,7.4)}=28.6$, $p=0.0005$	$F_{(1,5)}=2.0$, $p=0.21$	$F_{(1.5,7.3)}=2.2$, $p=0.18$
1.0 mg/kg	$F_{(1.9,11.4)}=27.8$, $p<0.0001$	$F_{(1,6)}=1.8$, $p=0.23$	$F_{(1.6, 8.5)}=2.0$, $p=41$
1.8 mg/kg	$F_{(1.3,7.8)}=90.0$, $p<0.0001$	$F_{(1,6)}=5.0$, $p=0.068$	$F_{(1.7,9.6)}=2.3$, $p=0.15$
3.2 mg/kg	$F_{(2.2,13.4)}=56.7$, $p<0.0001$	$F_{(1,6)}=2.1$, $p=0.20$	$F_{(1.7,10.5)}=0.75$, $p=0.48$
5.6 mg/kg	$F_{(1.7,6.8)}=50.0$, $p<0.0001$	$F_{(1,4)}=1.7$, $p=0.35$	$F_{(1.4,5.3)}=0.88$, $p=0.35$
Cocaine reinforcers taken			
Vehicle	$F_{(1.2,7.0)}=29.0$, $p=0.0008$	$F_{(1,6)}=6.7$, $p=0.04$	$F_{(1.5,8.7)}=7.5$, $p=0.02$
0.32 mg/kg	$F_{(1.4,7.4)}=11.6$, $p=0.007$	$F_{(1,5)}=3.1$, $p=0.14$	$F_{(1.7,8.5)}=2.3$, $p=0.16$
1.0 mg/kg	$F_{(1.5,9.3)}=18.3$, $p=0.0009$	$F_{(1,6)}=2.3$, $p=0.18$	$F_{(1.9,11.5)}=2.4$, $p=0.13$
1.8 mg/kg	$F_{(1.3,7.6)}=42.3$, $p=0.0002$	$F_{(1,6)}=8.5$, $p=0.03$	$F_{(1.7,10.0)}=2.2$, $p=0.16$
3.2 mg/kg	$F_{(2.0,11.8)}=31.1$, $p<0.0001$	$F_{(1,6)}=3.8$, $p=0.10$	$F_{(1.4,8.7)}=1.8$, $p=0.22$
5.6 mg/kg	$F_{(1.6,6.4)}=31.7$, $p=0.0006$	$F_{(1,4)}=1.0$, $p=0.37$	$F_{(1.8,7.3)}=1.2$, $p=0.35$
Liquid food reinforcers taken			
Vehicle	$F_{(1.1,6.5)}=45.3$, $p=0.0003$	$F_{(1,6)}=9.1$, $p=0.02$	$F_{(1.4,8.0)}=7.6$, $p=0.02$
0.32 mg/kg	$F_{(1.9,9.6)}=15.3$, $p=0.001$	$F_{(1,5)}=3.3$, $p=0.13$	$F_{(1.4,6.9)}=1.8$, $p=0.23$
1.0 mg/kg	$F_{(1.9,11.5)}=31.1$, $p<0.0001$	$F_{(1,6)}=0.12$, $p=0.74$	$F_{(1.5,9.2)}=2.3$, $p=0.16$
1.8 mg/kg	$F_{(2.5,15.2)}=43.8$, $p<0.0001$	$F_{(1,6)}=0.97$, $p=0.36$	$F_{(2.1,12.4)}=2.8$, $p=0.10$
3.2 mg/kg	$F_{(2.0,12.2)}=49.1$, $p<0.0001$	$F_{(1,6)}=0.50$, $p=0.51$	$F_{(1.7,10.6)}=1.7$, $p=0.23$
5.6 mg/kg	$F_{(1.7,7.1)}=43.9$, $p<0.0001$	$F_{(1,4)}=1.8$, $p=0.26$	$F_{(1.3,5.3)}=0.74$, $p=0.47$
Responses per minute, all levers			
Vehicle	$F_{(1.6,9.8)}=9.7$, $p=0.006$	$F_{(1,6)}=2.9$, $p=0.14$	$F_{(1.9,11.2)}=0.74$, $p=0.49$
0.32 mg/kg	$F_{(1.4,8.4)}=5.4$, $p=0.04$	$F_{(1,6)}=0.63$, $p=0.46$	$F_{(1.4, 8.9)}=2.9$, $p=0.12$
1.0 mg/kg	$F_{(1.3,7.9)}=11.8$, $p=0.007$	$F_{(1,6)}=0.04$, $p=0.85$	$F_{(1.8,10.6)}=0.78$, $p=0.47$
1.8 mg/kg	$F_{(1.3,8.1)}=14.9$, $p<0.003$	$F_{(1,6)}=0.15$, $p=0.71$	$F_{(1.5,8.9)}=1.2$, $p=0.34$
3.2 mg/kg	$F_{(1.3,8.1)}=14.9$, $p=0.003$	$F_{(1,6)}=0.15$, $p=0.71$	$F_{(1.5,8.9)}=1.2$, $p=0.34$
5.6 mg/kg	$F_{(1.3,5.1)}=11.3$, $p=0.02$	$F_{(1,4)}=0.82$, $p=0.41$	$F_{(2.4,9.7)}=3.9$, $p=0.055$
Responses per minute, reinforcer selection levers			
Vehicle	$F_{(1.8,10.7)}=1.2$, $p=0.35$	$F_{(1,6)}=1.3$, $p=0.29$	$F_{(2.7,16.0)}=1.4$, $p=0.27$
0.32 mg/kg	$F_{(3.2,15.9)}=1.5$, $p=0.24$	$F_{(1,5)}=41.6$, $p=0.001$	$F_{(3.0,14.8)}=0.74$, $p=0.54$
1.0 mg/kg	$F_{(1.2,7.2)}=1.6$, $p=0.25$	$F_{(1,6)}=0.60$, $p=0.47$	$F_{(1.4,8.8)}=1.1$, $p=0.36$
1.8 mg/kg	$F_{(2.1,12.9)}=3.4$, $p=0.064$	$F_{(1,6)}=1.2$, $p=0.32$	$F_{(2.0,11.8)}=1.3$, $p=0.30$
3.2 mg/kg	$F_{(2.4,14.3)}=2.8$, $p=0.09$	$F_{(1,6)}=0.21$, $p=0.66$	$F_{(1.9,11.3)}=0.99$, $p=0.40$
5.6 mg/kg	$F_{(2.3,9.1)}=2.0$, $p=0.19$	$F_{(1,4)}=14.0$, $p=0.02$	$F_{(2.0,8.2)}=0.52$, $p=0.52$

Table S2D. ANOVA outcomes for cocaine dose-response functions with VU0152100 in CalDAG-GEFI knockout mice

	3-way ANOVA
Pretreatment	$F_{(1,42)}=19.4$, $p=0.0001$
Cocaine dose	$F_{(3,42)}=8.08$, $p=0.004$
CalDAG-GEFI genotype	$F_{(1,42)}=12.6$, $p=0.001$
Cocaine by pretreatment interaction	$F_{(3,42)}=4.28$, $p=0.02$
Cocaine by genotype interaction	$F_{(3,42)}=3.35$, $p=0.07$
Pretreatment by genotype interaction	$F_{(1,42)}=0.25$, $p=0.62$
3-way interaction	$F_{(3,42)}=0.57$, $p=0.58$