

**Table 1A: Self-Administration Nose Pokes**

Model	Description
Self-Administration (Active/Inactive Nose Poke) × Reward × Day	GLMM with full interactions and subject as random effect; Post-hoc Multiple Pairwise Comparisons

**Fixed Effects**

Term	Estimate	SE	z	p-value	Sig
Intercept	3.182	0.207	15.36	< 0.0001	****
Nose Poke (Active vs. Inactive)	1.574	0.258	6.11	< 0.0001	****
Reward (Sucrose vs. Cocaine)	0.865	0.273	3.16	0.0016	**
Session (Day)	0.030	0.014	2.12	0.0344	*
Sex (Male vs Female)	0.013	0.302	0.04	0.9656	ns
Nose Poke × Reward	-0.523	0.354	-1.48	0.1391	ns
Nose Poke × Session	-0.010	0.021	-0.50	0.6187	ns
Reward × Session	-0.021	0.021	-1.00	0.3188	ns
Nose Poke × Sex	0.050	0.373	0.13	0.8942	ns
Reward × Sex	-0.902	0.386	-2.34	0.0194	*
Session × Sex	0.021	0.022	0.98	0.3284	ns
Nose Poke × Reward × Session	0.017	0.030	0.59	0.5565	ns
Nose Poke × Reward × Sex	0.422	0.503	0.84	0.4011	ns
Nose Poke × Session × Sex	-0.037	0.030	-1.24	0.2168	ns
Reward × Session × Sex	-0.001	0.030	-0.04	0.9648	ns
Nose Poke × Reward × Session × Sex	0.033	0.042	0.78	0.4325	ns

**Random Effects**

Group	Variance	SD
Mouse	0.0511	0.2260531

**Post-hoc Multiple Pairwise Comparison: Nose Poke × Reward × Sex**

Reward	Sex	Contrast	Estimate	SE	z	adj. p value	Sig
Cocaine	Female	Active - Inactive	-1.466	0.155	-9.46	< 0.0001	****
Sucrose	Female	Active - Inactive	-1.126	0.154	-7.29	< 0.0001	****
Cocaine	Male	Active - Inactive	-1.122	0.153	-7.33	< 0.0001	****
Sucrose	Male	Active - Inactive	-1.552	0.154	-10.10	< 0.0001	****

**Table 1B: Self-Administration Reward Deliveries**

<b>Model</b>		<b>Description</b>					
Delivery (Infusion/Pellet) × Session × Sex		GLMM with full interactions and subject as random effect; Post-hoc Multiple Pairwise Comparisons					
<b>Fixed Effects</b>							
<b>Term</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>p-value</b>	<b>Sig</b>		
Intercept	3.738	0.133	28.03	< 0.0001	****		
Reward (Sucrose vs. Cocaine)	-0.226	0.174	-1.30	0.1943	ns		
Session (Day)	0.009	0.019	0.48	0.6341	ns		
Sex (Male vs. Female)	-0.069	0.188	-0.37	0.7142	ns		
Reward × Session	0.073	0.026	2.74	0.0061	**		
Reward × Sex	0.070	0.247	0.28	0.7771	ns		
Session × Sex	0.001	0.027	0.03	0.9789	ns		
Reward × Session × Sex	-0.011	0.037	-0.30	0.7637	ns		
<b>Random Effects</b>							
<b>Group</b>	<b>Variance</b>		<b>SD</b>				
Mouse	0.0223		0.1493318				
<b>Post-hoc Multiple Pairwise Comparison: Reward × Sex × Session</b>							
<b>Session</b>	<b>Sex</b>	<b>Contrast</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>adj. p value</b>	<b>Sig</b>
1	Female	Cocaine - Sucrose	0.154	0.153	1.01	0.3147	ns
1	Male	Cocaine - Sucrose	0.095	0.153	0.62	0.5349	ns
2	Female	Cocaine - Sucrose	0.081	0.133	0.61	0.5430	ns
2	Male	Cocaine - Sucrose	0.034	0.133	0.25	0.8009	ns
3	Female	Cocaine - Sucrose	0.008	0.116	0.07	0.9431	ns
3	Male	Cocaine - Sucrose	-0.028	0.116	-0.24	0.8113	ns
4	Female	Cocaine - Sucrose	-0.064	0.103	-0.62	0.5326	ns
4	Male	Cocaine - Sucrose	-0.089	0.103	-0.86	0.3884	ns
5	Female	Cocaine - Sucrose	-0.137	0.096	-1.43	0.1533	ns
5	Male	Cocaine - Sucrose	-0.151	0.096	-1.57	0.1174	ns
6	Female	Cocaine - Sucrose	-0.210	0.096	-2.19	0.0286	*
6	Male	Cocaine - Sucrose	-0.212	0.096	-2.21	0.0273	*
7	Female	Cocaine - Sucrose	-0.282	0.103	-2.75	0.0060	**

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<b>Session</b>	<b>Sex</b>	<b>Contrast</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>adj. p value</b>	<b>Sig</b>
7	Male	Cocaine - Sucrose	-0.273	0.103	-2.65	0.0079	**
8	Female	Cocaine - Sucrose	-0.355	0.115	-3.07	0.0021	**
8	Male	Cocaine - Sucrose	-0.335	0.116	-2.89	0.0038	**
9	Female	Cocaine - Sucrose	-0.428	0.132	-3.23	0.0012	**
9	Male	Cocaine - Sucrose	-0.396	0.133	-2.99	0.0028	**
10	Female	Cocaine - Sucrose	-0.500	0.152	-3.29	0.0010	***
10	Male	Cocaine - Sucrose	-0.457	0.152	-3.00	0.0027	**

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**Table 1C: Extinction Nose Pokes**

Model		Description					
Extinction (Cocaine/Sucrose Nose Poke) × Session × Sex		GLMM with full interactions and subject as random effect; Post-hoc Multiple Pairwise Comparisons					
Fixed Effects							
Term	Estimate	SE	z	p-value	Sig		
Intercept	3.630	0.220	16.51	< 0.0001	****		
Nose Poke (Sucrose vs. Cocaine)	0.387	0.198	1.96	0.0505	.		
Session (Day)	-0.089	0.016	-5.45	< 0.0001	****		
Sex (Male vs Female)	-0.611	0.312	-1.96	0.0502	.		
Nose Poke × Session	-0.046	0.023	-1.99	0.0464	*		
Nose Poke × Sex	0.099	0.281	0.35	0.7244	ns		
Session × Sex	0.052	0.023	2.23	0.0258	*		
Nose Poke × Session × Sex	-0.047	0.033	-1.44	0.1495	ns		
Random Effects							
Group	Variance	SD					
Mouse	0.2576	0.5075431					
Post hoc Multiple Pairwise Comparison: Nose Poke × Sex × Session							
Session	Sex	Contrast	Estimate	SE	z	FDR-adjusted p-value	Sig
1	Female	Sucrose - Cocaine Nose Poke	-0.341	0.184	-1.86	0.0632	.
1	Male	Sucrose - Cocaine Nose Poke	-0.393	0.185	-2.12	0.0336	*
2	Female	Sucrose - Cocaine Nose Poke	-0.295	0.171	-1.72	0.0848	.
2	Male	Sucrose - Cocaine Nose Poke	-0.300	0.172	-1.74	0.0822	.
3	Female	Sucrose - Cocaine Nose Poke	-0.249	0.161	-1.55	0.1223	ns
3	Male	Sucrose - Cocaine Nose Poke	-0.207	0.162	-1.27	0.2032	ns
4	Female	Sucrose - Cocaine Nose Poke	-0.203	0.154	-1.32	0.1871	ns
4	Male	Sucrose - Cocaine Nose Poke	-0.114	0.155	-0.73	0.4644	ns
5	Female	Sucrose - Cocaine Nose Poke	-0.157	0.150	-1.05	0.2947	ns
5	Male	Sucrose - Cocaine Nose Poke	-0.020	0.151	-0.14	0.8926	ns
6	Female	Sucrose - Cocaine Nose Poke	-0.112	0.150	-0.74	0.4566	ns
6	Male	Sucrose - Cocaine Nose Poke	0.073	0.151	0.48	0.6300	ns
7	Female	Sucrose - Cocaine Nose Poke	-0.066	0.153	-0.43	0.6678	ns

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<b>Session</b>	<b>Sex</b>	<b>Contrast</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>FDR-adjusted p-value</b>	<b>Sig</b>
7	Male	Sucrose - Cocaine Nose Poke	0.166	0.154	1.08	0.2817	ns
8	Female	Sucrose - Cocaine Nose Poke	-0.020	0.159	-0.12	0.9016	ns
8	Male	Sucrose - Cocaine Nose Poke	0.259	0.161	1.61	0.1068	ns
9	Female	Sucrose - Cocaine Nose Poke	0.026	0.169	0.16	0.8764	ns
9	Male	Sucrose - Cocaine Nose Poke	0.352	0.170	2.07	0.0384	*
10	Female	Sucrose - Cocaine Nose Poke	0.072	0.180	0.40	0.6893	ns
10	Male	Sucrose - Cocaine Nose Poke	0.445	0.182	2.45	0.0144	*

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**Table 1D: Self-Administration vs. Extinction Phases (Active Nose Poke)**

<b>Model</b>		<b>Description</b>					
Active Nose Poke (SA/EXT) × Reward × Sex		GLMM with full interactions and subject as random effect; Post-hoc Multiple Pairwise Comparisons					
<b>Fixed Effects</b>							
<b>Term</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>p-value</b>	<b>Sig</b>		
Intercept	4.953	0.157	31.47	< 0.0001	****		
Active Nose Poke (SA vs. EXT)	-1.774	0.094	-18.95	< 0.0001	****		
Reward (Sucrose vs. Cocaine)	0.344	0.106	3.26	0.0011	**		
Sex (Male vs. Female)	-0.059	0.223	-0.27	0.7902	ns		
Phase × Reward	-0.196	0.132	-1.49	0.1362	ns		
Phase × Sex	-0.222	0.134	-1.66	0.0966	.		
Reward × Sex	-0.160	0.149	-1.07	0.2827	ns		
Phase × Reward × Sex	0.005	0.188	0.03	0.9774	ns		
<b>Random Effects</b>							
<b>Group</b>	<b>Variance</b>		<b>SD</b>				
Mouse	0.1727		0.4155719				
<b>Post-hoc Multiple Pairwise Comparison: Phase (SA/EXT) × Reward × Sex</b>							
<b>Reward</b>	<b>Sex</b>	<b>Contrast</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>FDR-adjusted p-value</b>	<b>Sig</b>
Cocaine	Female	EXT - SA	1.774	0.094	18.95	< 0.0001	****
Sucrose	Female	EXT - SA	1.970	0.094	21.06	< 0.0001	****
Cocaine	Male	EXT - SA	1.996	0.095	20.94	< 0.0001	****
Sucrose	Male	EXT - SA	2.187	0.095	23.02	< 0.0001	****

**Table 1E: Previous Day Extinction vs. Reinstatement (Nose Poke)**

<b>Model</b>	<b>Description</b>					
Phase (EXT/RST) × Nose Poke × Sex	GLMM with full interactions and subject as random effect; Post-hoc Multiple Pairwise Comparisons					
<b>Fixed Effects</b>						
<b>Term</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>p-value</b>	<b>Sig</b>	
Intercept	2.372	0.272	8.73	<0.0001	****	
RST vs EXT	0.816	0.260	3.14	0.0017	**	
Nose Poke: Sucrose vs Cocaine	-0.190	0.272	-0.70	0.4848	ns	
Sex: Male vs Female	-0.002	0.385	-0.01	0.9958	ns	
EXT × Nose Poke	-0.070	0.391	-0.18	0.8580	ns	
C-RST × Nose Poke	-0.968	0.380	-2.55	0.0108	*	
S-RST × Nose Poke	1.486	0.369	4.03	<0.0001	****	
EXT × Sex	-0.478	0.477	-1.00	0.3168	ns	
C-RST × Sex	0.103	0.368	0.28	0.7786	ns	
S-RST × Sex	-0.573	0.473	-1.21	0.2263	ns	
Nose Poke × Sex	-0.251	0.392	-0.64	0.5208	ns	
EXT × Nose Poke × Sex	0.625	0.565	1.10	0.2693	ns	
C-RST × Nose Poke × Sex	0.212	0.541	0.39	0.6956	ns	
S-RST × Nose Poke × Sex	0.509	0.539	0.95	0.3442	ns	
<b>Random Effects</b>						
<b>Group</b>	<b>Variance</b>		<b>SD</b>			
Mouse	0.1738380		0.4169388			
<b>Post hoc Multiple Pairwise Comparison: Phase (EXT-C, RST-C, EXT-S, RST-S) × Nose Poke × Sex</b>						
<b>Sex</b>	<b>contrast</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>adj. p-value</b>	<b>Sig</b>
Female	(EXT-C Cocaine) - (EXT-S Cocaine)	0.139	0.332	0.42	0.7556	ns
Female	(EXT-C Cocaine) - (C-RST Cocaine)	-0.816	0.260	-3.14	0.0048	**
Female	(EXT-C Cocaine) - (S-RST Cocaine)	-0.100	0.328	-0.30	0.8192	ns
Female	(EXT-C Cocaine) - (EXT-C Sucrose)	0.190	0.272	0.70	0.6464	ns
Female	(EXT-C Cocaine) - (EXT-S Sucrose)	0.399	0.338	1.18	0.3927	ns
Female	(EXT-C Cocaine) - (C-RST Sucrose)	0.341	0.277	1.23	0.3824	ns
Female	(EXT-C Cocaine) - (S-RST Sucrose)	-1.396	0.317	-4.40	< 0.0001	****
Female	(EXT-S Cocaine) - (C-RST Cocaine)	-0.956	0.323	-2.96	0.0079	**

Sex	contrast	Estimate	SE	z	adj. p-value	Sig
Female	(EXT-S Cocaine) - (S-RST Cocaine)	-0.239	0.270	-0.88	0.5346	ns
Female	(EXT-S Cocaine) - (EXT-C Sucrose)	0.050	0.335	0.15	0.8805	ns
Female	(EXT-S Cocaine) - (EXT-S Sucrose)	0.260	0.282	0.92	0.5346	ns
Female	(EXT-S Cocaine) - (C-RST Sucrose)	0.201	0.338	0.60	0.6709	ns
Female	(EXT-S Cocaine) - (S-RST Sucrose)	-1.535	0.257	-5.97	< 0.0001	****
Female	(C-RST Cocaine) - (S-RST Cocaine)	0.717	0.319	2.25	0.0574	.
Female	(C-RST Cocaine) - (EXT-C Sucrose)	1.006	0.264	3.81	0.0005	***
Female	(C-RST Cocaine) - (EXT-S Sucrose)	1.215	0.329	3.69	0.0007	***
Female	(C-RST Cocaine) - (C-RST Sucrose)	1.157	0.267	4.34	< 0.0001	****
Female	(C-RST Cocaine) - (S-RST Sucrose)	-0.580	0.308	-1.88	0.1292	ns
Female	(S-RST Cocaine) - (EXT-C Sucrose)	0.289	0.331	0.87	0.5346	ns
Female	(S-RST Cocaine) - (EXT-S Sucrose)	0.499	0.279	1.79	0.1482	ns
Female	(S-RST Cocaine) - (C-RST Sucrose)	0.441	0.334	1.32	0.3498	ns
Female	(S-RST Cocaine) - (S-RST Sucrose)	-1.296	0.250	-5.18	< 0.0001	****
Female	(EXT-C Sucrose) - (EXT-S Sucrose)	0.209	0.341	0.61	0.6709	ns
Female	(EXT-C Sucrose) - (C-RST Sucrose)	0.151	0.279	0.54	0.6861	ns
Female	(EXT-C Sucrose) - (S-RST Sucrose)	-1.586	0.321	-4.94	< 0.0001	****
Female	(EXT-S Sucrose) - (C-RST Sucrose)	-0.058	0.344	-0.17	0.8805	ns
Female	(EXT-S Sucrose) - (S-RST Sucrose)	-1.795	0.266	-6.76	< 0.0001	****
Female	(C-RST Sucrose) - (S-RST Sucrose)	-1.737	0.324	-5.36	< 0.0001	****
Male	(EXT-C Cocaine) - (EXT-S Cocaine)	0.617	0.343	1.80	0.1548	ns
Male	(EXT-C Cocaine) - (C-RST Cocaine)	-0.920	0.261	-3.53	0.0011	**
Male	(EXT-C Cocaine) - (S-RST Cocaine)	0.473	0.341	1.38	0.2908	ns
Male	(EXT-C Cocaine) - (EXT-C Sucrose)	0.441	0.283	1.56	0.2368	ns
Male	(EXT-C Cocaine) - (EXT-S Sucrose)	0.504	0.342	1.47	0.2620	ns
Male	(EXT-C Cocaine) - (C-RST Sucrose)	0.277	0.277	1.00	0.5090	ns
Male	(EXT-C Cocaine) - (S-RST Sucrose)	-1.081	0.322	-3.36	0.0018	**
Male	(EXT-S Cocaine) - (C-RST Cocaine)	-1.537	0.334	-4.61	< 0.0001	****
Male	(EXT-S Cocaine) - (S-RST Cocaine)	-0.144	0.295	-0.49	0.7286	ns
Male	(EXT-S Cocaine) - (EXT-C Sucrose)	-0.176	0.353	-0.50	0.7286	ns
Male	(EXT-S Cocaine) - (EXT-S Sucrose)	-0.113	0.295	-0.38	0.7847	ns
Male	(EXT-S Cocaine) - (C-RST Sucrose)	-0.340	0.347	-0.98	0.5090	ns
Male	(EXT-S Cocaine) - (S-RST Sucrose)	-1.698	0.271	-6.27	< 0.0001	****

<b>Sex</b>	<b>contrast</b>	<b>Estimate</b>	<b>SE</b>	<b>z</b>	<b>adj. p-value</b>	<b>Sig</b>
Male	(C-RST Cocaine) - (S-RST Cocaine)	1.393	0.332	4.19	< 0.0001	****
Male	(C-RST Cocaine) - (EXT-C Sucrose)	1.361	0.274	4.97	< 0.0001	****
Male	(C-RST Cocaine) - (EXT-S Sucrose)	1.423	0.332	4.29	< 0.0001	****
Male	(C-RST Cocaine) - (C-RST Sucrose)	1.197	0.263	4.56	< 0.0001	****
Male	(C-RST Cocaine) - (S-RST Sucrose)	-0.161	0.311	-0.52	0.7286	ns
Male	(S-RST Cocaine) - (EXT-C Sucrose)	-0.032	0.351	-0.09	0.9284	ns
Male	(S-RST Cocaine) - (EXT-S Sucrose)	0.031	0.295	0.10	0.9284	ns
Male	(S-RST Cocaine) - (C-RST Sucrose)	-0.195	0.346	-0.57	0.7286	ns
Male	(S-RST Cocaine) - (S-RST Sucrose)	-1.554	0.273	-5.69	< 0.0001	****
Male	(EXT-C Sucrose) - (EXT-S Sucrose)	0.062	0.351	0.18	0.9248	ns
Male	(EXT-C Sucrose) - (C-RST Sucrose)	-0.164	0.288	-0.57	0.7286	ns
Male	(EXT-C Sucrose) - (S-RST Sucrose)	-1.523	0.331	-4.59	< 0.0001	****
Male	(EXT-S Sucrose) - (C-RST Sucrose)	-0.226	0.345	-0.66	0.7286	ns
Male	(EXT-S Sucrose) - (S-RST Sucrose)	-1.585	0.270	-5.87	< 0.0001	****
Male	(C-RST Sucrose) - (S-RST Sucrose)	-1.359	0.325	-4.18	< 0.0001	****

**Table 1F: Fluorescent-Activated Cell Sorting (FACS)**

<b>Model</b>	<b>Description</b>					
Ensemble Size (Condition) × Region × Sex	Three-way ANOVA with full interactions; Post-hoc Multiple Pairwise Comparisons					
<b>Fixed Effects</b>						
<b>Effect</b>	<b>Sum Sq</b>	<b>Mean Sq</b>	<b>F value</b>	<b>p-value</b>	<b>Sig</b>	
Condition	588.96	294.48	38.50	<0.0001	****	
Region	53.29	53.29	6.97	0.0144	*	
Sex	10.39	10.39	1.36	0.2553	ns	
Condition × Region	67.66	33.83	4.42	0.0232	*	
Condition × Sex	8.53	4.27	0.56	0.5798	ns	
Region × Sex	0.24	0.24	0.03	0.8618	ns	
Condition × Region × Sex	7.48	3.74	0.49	0.6192	ns	
Residuals	183.59	7.65			ns	
<b>Post hoc pairwise comparisons: Condition × Region</b>						
<b>Region</b>	<b>contrast</b>	<b>estimate</b>	<b>SE</b>	<b>t</b>	<b>adj. p-value</b>	<b>Sig</b>
NAc	C - O	3.07	1.6	1.92	0.1550	ns
NAc	C - S	-9.59	1.6	-6.00	<0.0001	****
NAc	O - S	-12.65	1.6	-7.92	<0.0001	****
mPFC	C - O	2.64	1.6	1.65	0.2431	ns
mPFC	C - S	-3.99	1.6	-2.50	0.0496	*
mPFC	O - S	-6.63	1.6	-4.16	0.0010	**

**Table 1G: Reinstatement (Nose Poke) of Pooled Samples**

<b>Model</b>	<b>Description</b>	
Nose Poke x Phase (C-RST; S-RST) Sex x Replicate	GLMM Likelihood Ratio Test for replicate as random effect	
<b>Random Effects</b>		
<b>Effect</b>	<b>X<sup>2</sup></b>	<b>p-value</b>
Replicate	1.53	0.4652