

Figure S1| Systemic administration of MDMA does not alter novel object interaction in four mouse models for ASD. **A** Quantification of novel object interaction in control and *Sert-Cre^{+/+}:16p11.2^{flx/flx}* mice with systemic administration of vehicle or MDMA ($F_{1,42}=0.09315$, $P=0.7617$, $n=20-24$). If error bars are not clearly visible, they are smaller than the symbol used to represent the s.e.m. **B** Quantification of novel object interaction in control and *Cntnap2^{-/-}* mice with systemic administration of vehicle or MDMA ($F_{1,33}=0.2790$, $P=0.6009$, $n=16-19$). **C** Quantification of novel object interaction in control and *Fmr1^{-/y, -/-}* mice with systemic administration of vehicle or MDMA ($F_{1,36}=0.0018$, $P=0.9668$, $n=19$). **D** Quantification of novel object interaction in control and VPA mice with systemic administration of vehicle or MDMA ($F_{1,30}=0.0516$, $P=0.8219$, $n=15-17$). Data are mean \pm s.e.m. Two-way ANOVA.

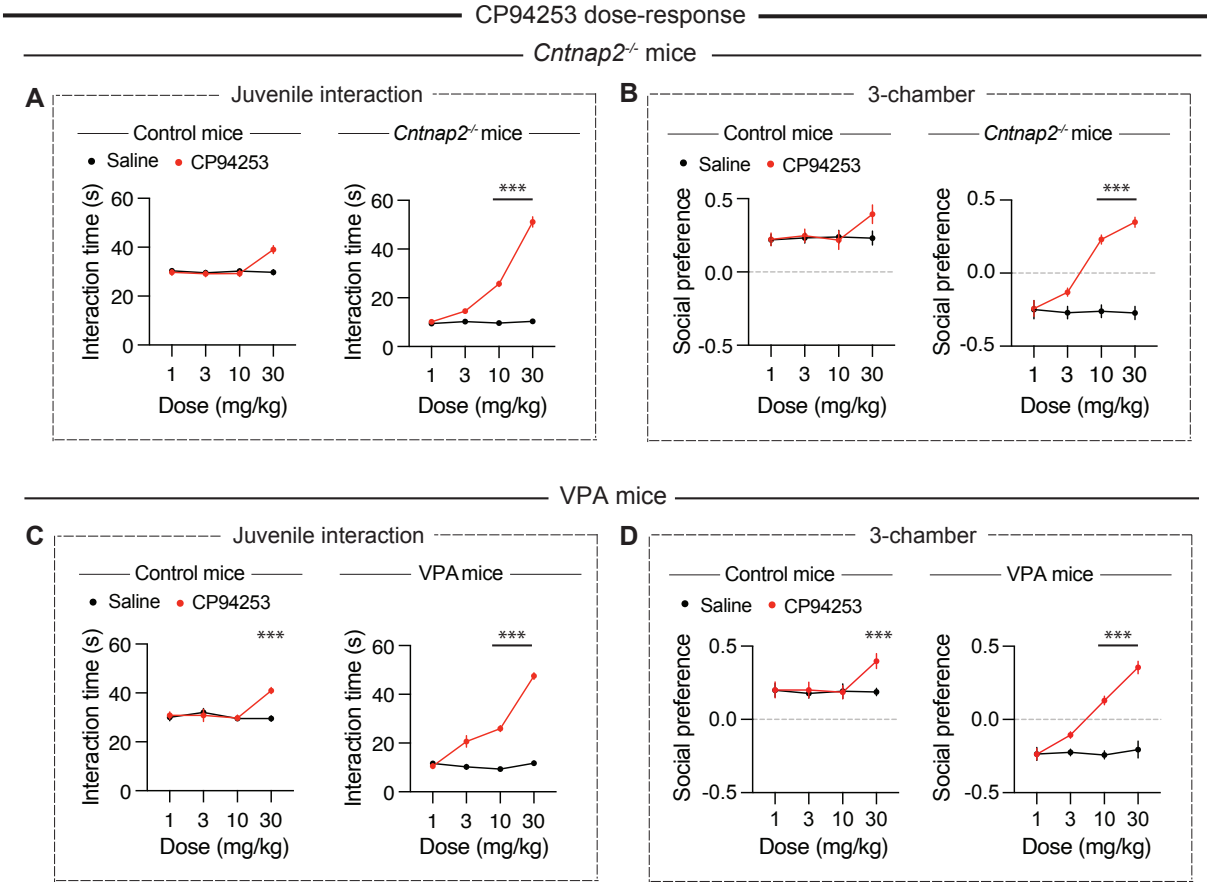


Figure S2| CP-94,253 administration dose-dependently reverses social deficits present in *Cntnap2*^{-/-} and VPA mice. **A** Quantification of juvenile interaction in control (left) and *Cntnap2*^{-/-} (right) mice with systemic administration of vehicle or a progressive dose series of CP-94,253 (1, 3, 10, and 30 mg/kg) ($F_{9,156}=58.62$, $P<0.001$, $n=14$). If error bars are not clearly visible, they are smaller than the symbol used to represent the s.e.m. **B** Quantification of 3-chamber sociability in control (left) and *Cntnap2*^{-/-} (right) mice with systemic administration of vehicle or a progressive dose series of CP-94,253 (1, 3, 10, and 30 mg/kg) ($F_{9,180}=9.563$, $P<0.001$, $n=14$). **C** Quantification of juvenile interaction in control (left) and VPA (right) mice with systemic administration of vehicle or one dose of CP-94,253 (1, 3, 10, or 30 mg/kg) ($F_{7,100}=50.76$, $P<0.001$, $n=13-14$). **D** Quantification of 3-chamber sociability in control (left) and VPA (right) mice with systemic administration of vehicle or one dose of CP-94,253 (1, 3, 10, or 30 mg/kg) ($F_{7,100}=16.59$, $P<0.001$, $n=13-14$). Data are mean \pm s.e.m. *** $P<0.001$; two-way ANOVA with Sidak's multiple comparison post hoc test.

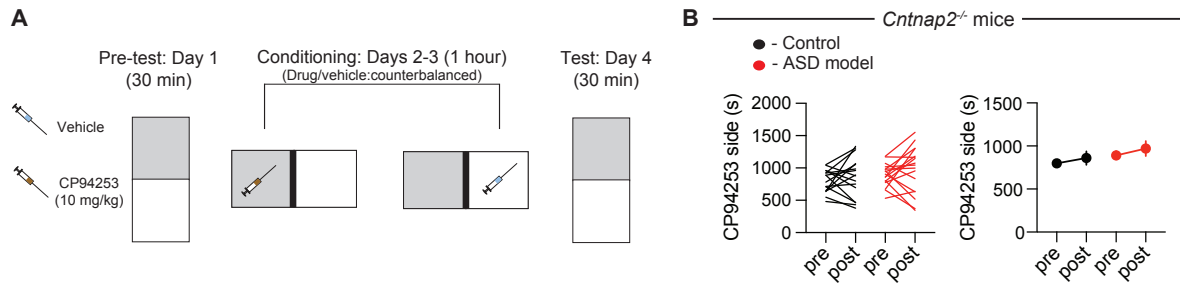


Figure S3| CP-94,253 administration in control and *Cntnap2*^{-/-} mice is not reinforcing. A Conditioned place preference (CPP) schematic using a single 1 hour pairing of context with CP-94,253 (10 mg/kg). If error bars are not clearly visible, they are smaller than the symbol used to represent the s.e.m. **B** Quantification of preference for CP-94,253-paired side, before and after conditioning in control (black) or *Cntnap2*^{-/-} (red) mice ($F_{1,30}=0.0087$, $P=0.9265$, $n=15-17$). Data are mean \pm s.e.m. Two-way ANOVA with Sidak's multiple comparison post hoc test.

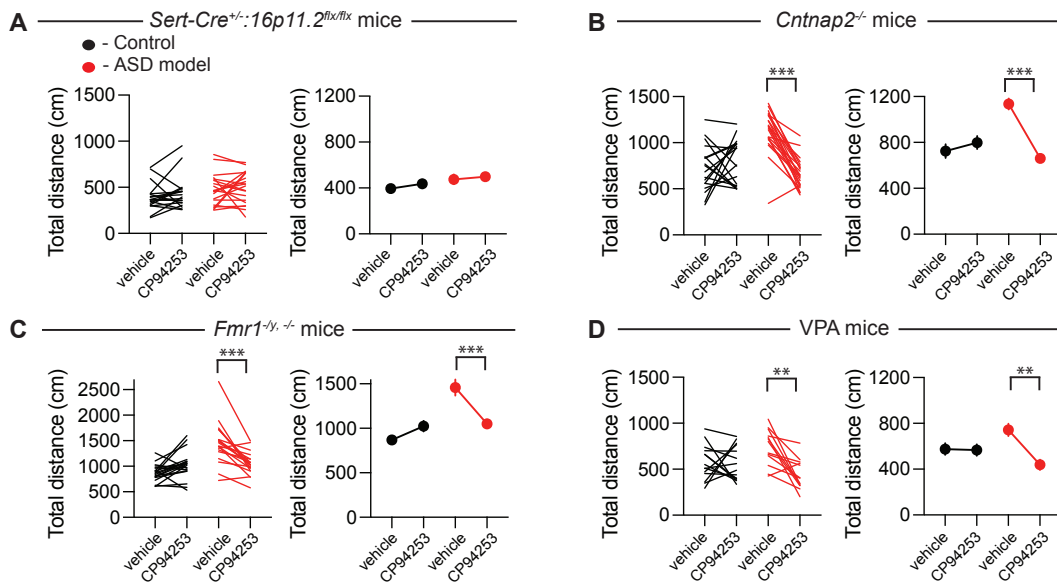


Figure S4| Systemic administration of CP-94,253 reverses hyperactivity present in three mouse models for ASD.

A Quantification of locomotion in control and *Sert-Cre^{+/-}:16p11.2^{flx/flx}* mice with systemic administration of vehicle or CP-94,253 ($F_{1,37}=0.1174$, $P=0.7338$, $n=19-20$). If error bars are not clearly visible, they are smaller than the symbol used to represent the s.e.m. **B** Quantification of locomotion in control and *Cntnap2^{-/-}* mice with systemic administration of vehicle or CP,94-253 ($F_{1,39}=35.62$, $P<0.001$, $n=18-23$). **C** Quantification of locomotion in control and *Fmr1^{-ly-/-}* mice with systemic administration of vehicle or CP-94,253 ($F_{1,38}=34.55$, $P<0.001$, $n=20$). **D** Quantification of locomotion in control and VPA mice with systemic administration of vehicle or CP-94,253 ($F_{1,25}=7.964$, $P<0.01$, $n=13-14$). Data are mean \pm s.e.m. ** $P<0.01$, *** $P<0.001$; two-way ANOVA with Sidak's multiple comparison post hoc test.

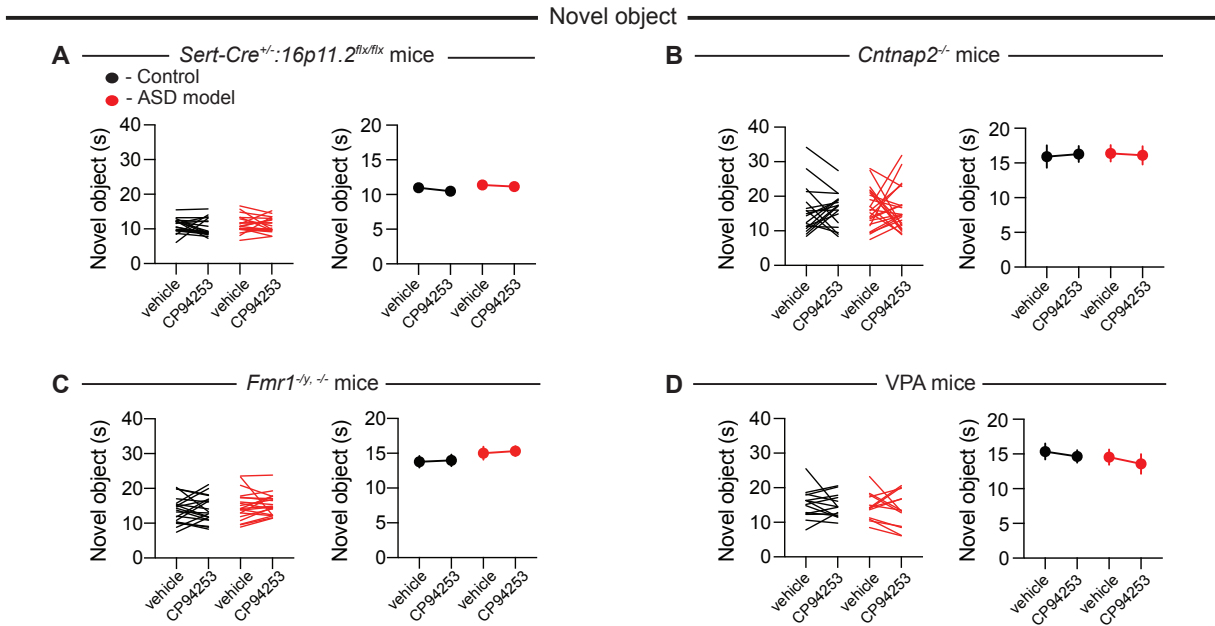


Figure S5| Systemic administration of CP-94,253 does not alter novel object interaction in four mouse models for ASD. A Quantification of novel object interaction in control and *Sert-Cre^{+/-}:16p11.2^{flx/flx}* mice with systemic administration of vehicle or CP-94,253 ($F_{1,37}=0.09797$, $P=0.7560$, $n=19-20$). If error bars are not clearly visible, they are smaller than the symbol used to represent the s.e.m. **B** Quantification of novel object interaction in control and *Cntnap2^{-/-}* mice with systemic administration of vehicle or CP,94-253 ($F_{1,39}=0.07297$, $P=0.7885$, $n=18-23$). **C** Quantification of novel object interaction in control and *Fmr1^{-ly, -/-}* mice with systemic administration of vehicle or CP-94,253 ($F_{1,38}=0.01163$, $P=0.9147$, $n=20$). **D** Quantification of novel object interaction in control and VPA mice with systemic administration of vehicle or CP-94,253 ($F_{1,25}=0.0195$, $P=0.8902$, $n=13-14$). Data are mean \pm s.e.m. Two-way ANOVA.

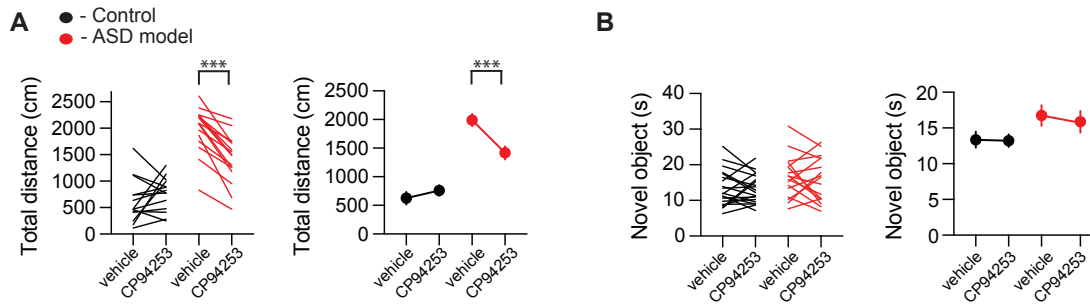


Figure S6 | Systemic administration of CP-94,253 reverses hyperactivity in *Actl6b*^{-/-} mice, but does not alter novel object interaction. **A Quantification of locomotion in control and *Actl6b*^{-/-} mice with systemic administration of vehicle or CP,94-253 ($F_{1,28}=28.06$, $P<0.001$, $n=14-16$). **B** Quantification of novel object interaction in control and *Actl6b*^{-/-} mice with systemic administration of vehicle or CP-94,253 ($F_{1,35}=0.1804$, $P=0.6736$, $n=17-20$). Data are mean \pm s.e.m. *** $P<0.001$; two-way ANOVA with Sidak's multiple comparison post hoc test.**

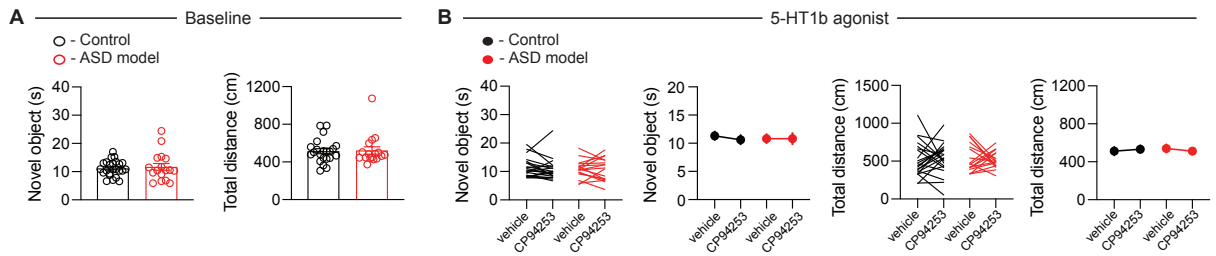


Figure S7| *Sert-Cre^{+/-}:Arid1b^{flx/+}* mice do not have alterations in baseline control behaviors or with systemic administration of CP-94,253. A *Sert-Cre^{+/-}:Arid1b^{flx/+}* does not alter novel objection interaction ($t_{39}=0.4200$, $P=0.6768$, $n=17-24$) or locomotion ($t_{37}=0.1892$, $P=0.8510$, $n=17-22$). B Quantification of novel object interaction ($F_{1,37}=0.4398$, $P=0.5113$, $n=17-22$) and locomotion ($F_{1,37}=0.3338$, $P=0.5669$, $n=17-22$) in control and *Sert-Cre^{+/-}:Arid1b^{flx/+}* mice with systemic administration of vehicle or CP-94,253. Data are mean \pm s.e.m. Two-way ANOVA with Sidak's multiple comparison post hoc test.

Table 1 ASD Model and Control Genotypes

Autism model	Autism model genotype cross	Control genotype
<i>Sert-Cre</i> ^{+/-} :16p11.2 ^{flx/flx}	B6N.129P2(Cg)-Igs13 ^{tm1Dolm} Igs14 ^{tm1Dolm} /J (homozygous , CD1 background) x Tg(Slc6a4-cre)ET33Gsat (heterozygous , C57BL/6)	<i>Sert-Cre</i> ^{-/-} :16p11.2 ^{flx/flx} littermates
<i>Cntnap2</i> ^{-/-}	B6.129(Cg)- <i>Cntnap2</i> ^{tm1Pele} /J	<i>Cntnap2</i> ^{+/+} littermates
Males: <i>Fmr1</i> ^{-/y} , Females: <i>Fmr1</i> ^{-/-}	B6.129P2- <i>Fmr1</i> ^{tm1Cgr} /J	Males: <i>Fmr1</i> ^{+/y} , Females: <i>Fmr1</i> ^{+/+}
VPA	C57BL/6 pups from pregnant females injected at E12.5 with 600mg/kg VPA	C57BL/6 pups from pregnant females injected at E12.5 with Saline
<i>Actl6b</i> ^{-/-}	B6.129S6- <i>Actl6b</i> ^{tm1Grc} /J	<i>Actl6b</i> ^{+/+}
<i>Sert-Cre</i> ^{+/-} : <i>Arid1b</i> ^{flx/+}	C57BL/6-Arid1bem2Hzhu/J (heterozygous) x Tg(Slc6a4-cre)ET33Gsat (heterozygous)	<i>Sert-Cre</i> ^{-/-} : <i>Arid1b</i> ^{flx/+} littermates

Table S2: Analysis of Experimentals Results by Sex

Figure	Autism Model	Behavior	Males		Females		Statistics				
			n (CON)	n (ASD)	n (CON)	n (ASD)	Statistical test	Post-hoc test	Factor	Test statistic	p-value
1B	<i>Sert-Cre^{+/+};16p11.2^{flx/flx}</i>	Juvenile Interaction	11	12	13	9	2-way ANOVA		Interaction	F (1, 41) = 0.9993	0.323
			11	12	13	9	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 5.640, df = 41	<0.0001
			11	12	13	9	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 7.30, df = 41	<0.0001
		3-Chamber	11	12	13	9	2-way ANOVA		Interaction	F (1, 39) = 1.88	0.178
			11	12	13	9	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 5.648, df = 39	<0.0001
11	12	13	9	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 5.869, df = 39	<0.0001			
1C	<i>Cntnap2^{-/-}</i>	Juvenile Interaction	9	14	9	9	2-way ANOVA		Interaction	F (1, 37) = 0.6227	0.4351
			9	14	9	9	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 7.346, df = 37	<0.0001
			9	14	9	9	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 2.202, df = 37	<0.0001
		3-Chamber	9	14	9	9	2-way ANOVA		Interaction	F (1, 37) = 0.1064	0.7461
			9	14	9	9	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 5.303, df = 37	<0.0001
9	14	9	9	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 6.337, df = 37	<0.0001			
1D	<i>Fmr1^{dy/-}</i>	Juvenile Interaction	10	10	10	10	2-way ANOVA		Interaction	F (1, 36) = 0.1695	0.683
			10	10	10	10	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 11.83, df = 36	<0.0001
			10	10	10	10	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 11.25, df = 36	<0.0001
		3-Chamber	10	10	10	10	2-way ANOVA		Interaction	F (1, 36) = 0.002345	0.9616
			10	10	10	10	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 3.486, df = 36	0.0078
10	10	10	10	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 3.417, df = 36	0.0095			
1E	Valproic Acid	Juvenile Interaction	9	8	5	5	2-way ANOVA		Interaction	F (1, 23) = 0.7730	0.3884
			9	8	5	5	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 3.681, df = 23	0.0074
			9	8	5	5	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 3.348, df = 23	0.0166
		3-Chamber	9	8	5	5	2-way ANOVA		Interaction	F (1, 23) = 3.428	0.077
			9	8	5	5	2-way ANOVA	Šídák's	CON:Females vs. ASD:Males	t = 4.240, df = 23	0.0019
9	8	5	5	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 4.865, df = 23	0.0004			
1F	<i>Sert-Cre^{+/+};16p11.2^{flx/flx}</i>	Novel Object	6	11	13	9	2-way ANOVA		Interaction	F (1, 35) = 0.02403	0.8777
		Locomotion	6	11	13	9	2-way ANOVA		Interaction	F (1, 35) = 0.5608	0.459
1G	<i>Cntnap2^{-/-}</i>	Novel Object	9	14	9	9	2-way ANOVA		Interaction	F (1, 37) = 0.01136	0.9157
		Locomotion	9	14	9	9	2-way ANOVA		Interaction	F (1, 37) = 1.391	0.2457
1H	<i>Fmr1^{dy/-}</i>	Novel Object	10	10	10	10	2-way ANOVA		Interaction	F (1, 36) = 0.01646	0.8986
		Locomotion	10	10	10	10	2-way ANOVA		Interaction	F (1, 36) = 7.971	0.0077
1I	Valproic Acid	Novel Object	9	8	5	5	2-way ANOVA		Interaction	F (1, 23) = 0.3724	0.5477
		Locomotion	9	8	5	5	2-way ANOVA		Interaction	F (1, 23) = 5.511	0.0279

2A	Sert-Cre ^{+/+} :16p11.2 ^{flx/flx}	Juvenile Interaction	12	12	12	8	3-way ANOVA		Drug x Genotype	F (1, 40) = 42.46	<0.0001
			12	12	12	8	3-way ANOVA		Drug x Sex	F (1, 40) = 1.101	0.3003
			12	12	12	8	3-way ANOVA		Sex x Genotype	F (1, 40) = 0.08675	0.7699
			12	12	12	8	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 6.701, df = 40	<0.0001
			12	12	12	8	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 7.889, df = 40	<0.0001
		3-Chamber	12	12	12	8	3-way ANOVA		Drug x Genotype	F (1, 40) = 33.50	<0.0001
			12	12	12	8	3-way ANOVA		Drug x Sex	F (1, 40) = 1.686	0.2015
			12	12	12	8	3-way ANOVA		Sex x Genotype	F (1, 40) = 1.821	0.1848
			12	12	12	8	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 9.569, df = 40	<0.0001
			12	12	12	8	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 8.137, df = 40	<0.0001
2B	Cntnap2 ^{-/-}	Juvenile Interaction	10	7	9	9	3-way ANOVA		Drug x Genotype	F (1, 31) = 44.13	<0.0001
			10	7	9	9	3-way ANOVA		Drug x Sex	F (1, 31) = 0.1291	0.7218
			10	7	9	9	3-way ANOVA		Sex x Genotype	F (1, 31) = 0.2492	0.6211
			10	7	9	9	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 6.696, df = 31	<0.0001
			10	7	9	9	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 5.232, df = 31	0.0001
		3-Chamber	10	7	9	9	3-way ANOVA		Drug x Genotype	F (1, 31) = 2.043	0.1629
			10	7	9	9	3-way ANOVA		Drug x Sex	F (1, 31) = 0.1695	0.6834
			10	7	9	9	3-way ANOVA		Sex x Genotype	F (1, 31) = 0.1187	0.7328
			10	7	9	9	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 4.785, df = 31	0.0005
			10	7	9	9	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 4.723, df = 31	0.0006
2C	Fmr1 ^{-y,-/-}	Juvenile Interaction	9	9	10	10	3-way ANOVA		Drug x Genotype	F (1, 34) = 118.0	<0.0001
			9	9	10	10	3-way ANOVA		Drug x Sex	F (1, 34) = 0.4894	0.489
			9	9	10	10	3-way ANOVA		Sex x Genotype	F (1, 34) = 0.9973	0.325
			9	9	10	10	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 11.05, df = 34	<0.0001
			9	9	10	10	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 10.00, df = 34	<0.0001
		3-Chamber	9	9	10	10	3-way ANOVA		Drug x Genotype	F (1, 34) = 2.853	0.1003
			9	9	10	10	3-way ANOVA		Drug x Sex	F (1, 34) = 1.963	0.1703
			9	9	10	10	3-way ANOVA		Sex x Genotype	F (1, 34) = 1.221	0.2769
			9	9	10	10	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 3.542, df = 34	0.014
			9	9	10	10	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 5.321, df = 34	<0.0001
2D	Valproic Acid	Juvenile Interaction	9	8	8	7	3-way ANOVA		Drug x Genotype	F (1, 28) = 162.2	<0.0001
			9	8	8	7	3-way ANOVA		Drug x Sex	F (1, 28) = 0.1133	0.7389
			9	8	8	7	3-way ANOVA		Sex x Genotype	F (1, 28) = 4.693	0.039
			9	8	8	7	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 11.22, df = 28	<0.0001
			9	8	8	7	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 11.30, df = 28	<0.0001
		3-Chamber	9	8	8	7	3-way ANOVA		Drug x Genotype	F (1, 28) = 23.71	<0.0001
			9	8	8	7	3-way ANOVA		Drug x Sex	F (1, 28) = 0.7731	0.3867
			9	8	8	7	3-way ANOVA		Sex x Genotype	F (1, 28) = 0.9209	0.3454
			9	8	8	7	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 5.900, df = 28	<0.0001
			9	8	8	7	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 7.181, df = 28	<0.0001

3A	Sert-Cre ^{+/+} :16p11.2 ^{flx/flx}	Juvenile Interaction	11	12	13	9	3-way ANOVA		Drug x Genotype	F (1, 41) = 45.32	<0.0001
			11	12	13	9	3-way ANOVA		Drug x Sex	F (1, 41) = 1.011	0.3205
			11	12	13	9	3-way ANOVA		Sex x Genotype	F (1, 41) = 0.04931	0.8254
			11	12	13	9	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 4.156, df = 41	0.0019
			11	12	13	9	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 7.897, df = 41	<0.0001
		3-Chamber	11	10	13	9	3-way ANOVA		Drug x Genotype	F (1, 39) = 32.91	<0.0001
			11	10	13	9	3-way ANOVA		Drug x Sex	F (1, 39) = 0.06229	0.8042
			11	10	13	9	3-way ANOVA		Sex x Genotype	F (1, 39) = 1.178	0.2845
			11	10	13	9	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 5.382, df = 39	<0.0001
			11	10	13	9	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 5.233, df = 39	<0.0001
3B	Cntnap2 ^{-/-}	Juvenile Interaction	9	14	9	9	3-way ANOVA		Drug x Genotype	F (1, 37) = 27.99	<0.0001
			9	14	9	9	3-way ANOVA		Drug x Sex	F (1, 37) = 0.6202	0.436
			9	14	9	9	3-way ANOVA		Sex x Genotype	F (1, 37) = 0.1419	0.7085
			9	14	9	9	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 4.922, df = 37	0.0002
			9	14	9	9	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 7.024, df = 37	<0.0001
		3-Chamber	9	14	9	9	3-way ANOVA		Drug x Genotype	F (1, 37) = 54.44	<0.0001
			9	14	9	9	3-way ANOVA		Drug x Sex	F (1, 37) = 2.916	0.0961
			9	14	9	9	3-way ANOVA		Sex x Genotype	F (1, 37) = 1.984	0.1673
			9	14	9	9	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 9.196, df = 37	<0.0001
			9	14	9	9	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 6.590, df = 37	<0.0001
3C	Fmr1 ^{-y,-/-}	Juvenile Interaction	10	10	10	10	3-way ANOVA		Drug x Genotype	F (1, 36) = 67.46	<0.0001
			10	10	10	10	3-way ANOVA		Drug x Sex	F (1, 36) = 7.340	0.0103
			10	10	10	10	3-way ANOVA		Sex x Genotype	F (1, 36) = 0.3511	0.5572
			10	10	10	10	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 10.15, df = 36	<0.0001
			10	10	10	10	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 5.540, df = 36	<0.0001
		3-Chamber	9	9	10	10	3-way ANOVA		Drug x Genotype	F (1, 34) = 37.70	<0.0001
			9	9	10	10	3-way ANOVA		Drug x Sex	F (1, 34) = 0.1109	0.7411
			9	9	10	10	3-way ANOVA		Sex x Genotype	F (1, 34) = 0.1852	0.6697
			9	9	10	10	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 5.383, df = 34	<0.0001
			9	9	10	10	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 5.743, df = 34	<0.0001
3D	Valproic Acid	Juvenile Interaction	9	8	5	5	3-way ANOVA		Drug x Genotype	F (1, 23) = 9.261	0.0058
			9	8	5	5	3-way ANOVA		Drug x Sex	F (1, 23) = 0.0009178	0.9761
			9	8	5	5	3-way ANOVA		Sex x Genotype	F (1, 23) = 0.2986	0.59
			9	8	5	5	3-way ANOVA	Šídák's	saline:CON-F vs. saline:ASD-F	t = 3.637, df = 46	0.0083
			9	8	5	5	3-way ANOVA	Šídák's	saline:CON_M vs. saline:ASD-M	t = 4.104, df = 46	0.002
		3-Chamber	9	7	5	5	3-way ANOVA		Drug x Genotype	F (1, 22) = 8.626	0.0076
			9	7	5	5	3-way ANOVA		Drug x Sex	F (1, 22) = 0.5671	0.4594
			9	7	5	5	3-way ANOVA		Sex x Genotype	F (1, 22) = 0.7591	0.393
			9	7	5	5	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 3.352, df = 22	0.034
			9	7	5	5	3-way ANOVA	Šídák's	saline:CON-F vs. saline:ASD-F	t = 3.758, df = 44	0.006
						Šídák's	saline:CON_M vs. saline:ASD-M	t = 4.630, df = 44	0.0004		

4A	<i>Act16b</i> ^{-/-}	Juvenile Interaction	9	7	11	10	2-way ANOVA		Interaction	F (1, 33) = 0.07653	0.7838
			9	7	11	10	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 8.665, df = 33	<0.0001
			9	7	11	10	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 7.879, df = 33	<0.0001
		3-Chamber	9	7	11	10	2-way ANOVA		Interaction	F (1, 33) = 0.3609	0.5521
			9	7	11	10	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 11.60, df = 33	<0.0001
			9	7	11	10	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 9.263, df = 33	<0.0001
4B	<i>Act16b</i> ^{-/-}	Juvenile Interaction	12	6	8	11	3-way ANOVA		Drug x Genotype	F (1, 33) = 28.16	<0.0001
			12	6	8	11	3-way ANOVA		Drug x Sex	F (1, 33) = 0.007671	0.9307
			12	6	8	11	3-way ANOVA		Sex x Genotype	F (1, 33) = 0.5192	0.47363
			12	6	8	11	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 5.491, df = 33	<0.0001
			12	6	8	11	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 4.659, df = 33	0.0006
4C	<i>Act16b</i> ^{-/-}	3-Chamber	14	13	14	11	3-way ANOVA		Drug x Genotype	F (1, 48) = 16.32	0.0002
			14	13	14	11	3-way ANOVA		Drug x Sex	F (1, 48) = 0.6479	0.4248
			14	13	14	11	3-way ANOVA		Sex x Genotype	F (1, 48) = 0.04932	0.8252
			14	13	14	11	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 4.243, df = 48	0.0012
			14	13	14	11	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 5.112, df = 48	<0.0001
4D	<i>Sert-Cre</i> ^{+/-} ; <i>Arid1b</i> ^{flx/+}	Juvenile Interaction	14	12	10	5	2-way ANOVA		Interaction	F (1, 37) = 0.01947	0.8898
			14	12	10	5	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 5.138, df = 37	<0.0001
			14	12	10	5	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 6.914, df = 37	<0.0001
		3-Chamber	14	12	10	5	2-way ANOVA		Interaction	F (1, 37) = 0.2348	0.6308
			14	12	10	5	2-way ANOVA	Šídák's	CON:Females vs. ASD:Females	t = 3.924, df = 37	0.0022
			14	12	10	5	2-way ANOVA	Šídák's	CON:Males vs. ASD:Males	t = 6.294, df = 37	<0.0001
4E	<i>Sert-Cre</i> ^{+/-} ; <i>Arid1b</i> ^{flx/+}	Juvenile Interaction	14	12	8	5	3-way ANOVA		Drug x Genotype	F (1, 35) = 40.08	<0.0001
			14	12	8	5	3-way ANOVA		Drug x Sex	F (1, 35) = 0.09725	0.757
			14	12	8	5	3-way ANOVA		Sex x Genotype	F (1, 35) = 0.1138	0.7379
			14	12	8	5	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 4.431, df = 35	0.0011
			14	12	8	5	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 8.212, df = 35	<0.0001
4F	<i>Sert-Cre</i> ^{+/-} ; <i>Arid1b</i> ^{flx/+}	3-Chamber	14	12	8	5	3-way ANOVA		Drug x Genotype	F (1, 35) = 22.49	<0.0001
			14	12	8	5	3-way ANOVA		Drug x Sex	F (1, 35) = 0.2187	0.6429
			14	12	8	5	3-way ANOVA		Sex x Genotype	F (1, 35) = 0.7598	0.3893
			14	12	8	5	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 4.194, df = 35	0.0021
			14	12	8	5	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 6.365, df = 35	<0.0001
S1A	<i>Sert-Cre</i> ^{+/-} ; <i>16p11.2</i> ^{flx/flx}	Novel Object	12	12	12	8	3-way ANOVA		Drug x Genotype	F (1, 40) = 0.05997	0.8078
			12	12	12	8	3-way ANOVA		Drug x Sex	F (1, 40) = 0.6242	0.4342
			12	12	12	8	3-way ANOVA		Sex x Genotype	F (1, 40) = 0.006668	0.9353
S1B	<i>Cntnap2</i> ^{-/-}	Novel Object	10	7	9	9	3-way ANOVA		Drug x Genotype	F (1, 31) = 0.1562	0.6954
			10	7	9	9	3-way ANOVA		Drug x Sex	F (1, 31) = 1.647	0.2088
			10	7	9	9	3-way ANOVA		Sex x Genotype	F (1, 31) = 0.8366	0.3674
S1C	<i>Fmr1</i> ^{+/y,-/-}	Novel Object	9	9	10	10	3-way ANOVA		Drug x Genotype	F (1, 34) = 0.005500	0.9413
			9	9	10	10	3-way ANOVA		Drug x Sex	F (1, 34) = 0.005872	0.9394
			9	9	10	10	3-way ANOVA		Sex x Genotype	F (1, 34) = 0.1865	0.6685
S1D	Valproic Acid	Novel Object	9	8	8	7	3-way ANOVA		Drug x Genotype	F (1, 28) = 0.04069	0.8416
			9	8	8	7	3-way ANOVA		Drug x Sex	F (1, 28) = 0.9374	0.3412
			9	8	8	7	3-way ANOVA		Sex x Genotype	F (1, 28) = 1.192	0.2842

S2A	<i>Cntnap2^{-/-}</i>	Juvenile Interaction	7		7		3-way ANOVA		Dose x Sex	F (3, 72) = 0.05920	0.981
			7		7		3-way ANOVA		Dose x Drug	F (3, 72) = 7.756	0.0001
			7		7		3-way ANOVA		Sex x Drug	F (1, 24) = 0.5218	0.4771
		Juvenile Interaction	7		7		3-way ANOVA		Dose x Sex	F (3, 72) = 0.9791	0.4075
			7		7		3-way ANOVA		Dose x Drug	F (3, 72) = 141.9	<0.0001
			7		7		3-way ANOVA		Sex x Drug	F (1, 24) = 0.1707	0.6832
			7		7		3-way ANOVA	Šídák's	10mg/kg Saline-F vs. Agonist-F	t = 9.249, df = 10	0.0006
			7		7		3-way ANOVA	Šídák's	10mg/kg Saline-M vs. Agonist-M	t = 8.534, df = 10	0.0072
			7		7		3-way ANOVA	Šídák's	30mg/kg Saline-F vs. Saline-M	t = 11.5, df = 10	0.0011
S2B	<i>Cntnap2^{-/-}</i>	3-Chamber	8		7		3-way ANOVA		Dose x Sex	F (3, 78) = 0.01065	0.9985
			8		7		3-way ANOVA		Dose x Drug	F (3, 78) = 1.292	0.283
			8		7		3-way ANOVA		Sex x Drug	F (1, 26) = 0.003820	0.9512
		3-Chamber	9		9		3-way ANOVA		Dose x Sex	F (3, 90) = 0.006087	0.9993
			9		9		3-way ANOVA		Dose x Drug	F (3, 90) = 21.60	<0.0001
			9		9		3-way ANOVA		Sex x Drug	F (1, 30) = 0.007317	0.9324
			9		9		3-way ANOVA	Šídák's	10mg/kg Saline-F vs. Agonist-F	t = 6.99, df = 14	0.0008
			9		9		3-way ANOVA	Šídák's	10mg/kg Saline-M vs. Agonist-M	t = 5.962, df = 13	0.0072
			9		9		3-way ANOVA	Šídák's	30mg/kg Saline-F vs. Saline-M	t = 6.497, df = 14	0.0018
S2C	Valproic Acid	Juvenile Interaction 1mg/kg	7	7	7	7	3-way ANOVA		Drug x Sex	F (1, 24) = 0.004838	0.9451
			7	7	7	7	3-way ANOVA		Drug x Genotype	F (1, 24) = 0.4113	0.5274
			7	7	7	7	3-way ANOVA		Sex x Genotype	F (1, 24) = 0.2546	0.6184
			7	7	7	7	3-way ANOVA	Šídák's	Saline-CON-F vs Saline-ASD-F	t = 10.35, df = 48	<0.0001
			7	7	7	7	3-way ANOVA	Šídák's	Saline-CON-M vs Saline-ASD-M	t = 9.603, df = 48	<0.0001
		Juvenile Interaction 3mg/kg	7	7	6	7	3-way ANOVA		Drug x Sex	F (1, 22) = 0.0006713	0.9796
			7	7	6	7	3-way ANOVA		Drug x Genotype	F (1, 22) = 12.04	0.0022
			7	7	6	7	3-way ANOVA		Sex x Genotype	F (1, 22) = 2.755e-005	0.9959
			7	7	6	7	3-way ANOVA	Šídák's	Saline-CON-F vs Saline-ASD-F	t = 7.565, df = 44	<0.0001
			7	7	6	7	3-way ANOVA	Šídák's	Saline-CON-M vs Saline-ASD-M	t = 8.072, df = 44	<0.0001
		Juvenile Interaction 10mg/kg	7	7	7	7	3-way ANOVA		Drug x Sex	F (1, 24) = 0.6842	0.4163
			7	7	7	7	3-way ANOVA		Drug x Genotype	F (1, 24) = 92.62	<0.0001
			7	7	7	7	3-way ANOVA		Sex x Genotype	F (1, 24) = 0.6452	0.4297
			7	7	7	7	3-way ANOVA	Šídák's	Saline-CON-F vs Saline-ASD-F	t = 9.549, df = 48	<0.0001
			7	7	7	7	3-way ANOVA	Šídák's	Saline-CON-M vs Saline-ASD-M	t = 10.27, df = 48	<0.0001
			7	7	7	7	3-way ANOVA	Šídák's	Saline-ASD-F vs Drug-ASD-F	t = 9.891, df = 24	<0.0001
			7	7	7	7	3-way ANOVA	Šídák's	Saline-ASD-M vs Drug-ASD-M	t = 9.190, df = 24	<0.0001
		Juvenile Interaction 30mg/kg	7	7	6	7	3-way ANOVA		Drug x Sex	F (1, 22) = 0.003555	0.953
			7	7	6	7	3-way ANOVA		Drug x Genotype	F (1, 22) = 137.9	<0.0001
			7	7	6	7	3-way ANOVA		Sex x Genotype	F (1, 22) = 0.07603	0.7853
			7	7	6	7	3-way ANOVA	Šídák's	Saline-CON-F vs Saline-ASD-F	t = 10.38, df = 44	<0.0001
			7	7	6	7	3-way ANOVA	Šídák's	Saline-CON-M vs Saline-ASD-M	t = 10.46, df = 44	<0.0001
			7	7	6	7	3-way ANOVA	Šídák's	Saline-ASD-F vs Drug-ASD-F	t = 23.76, df = 22	<0.0001
			7	7	6	7	3-way ANOVA	Šídák's	Saline-ASD-M vs Drug-ASD-M	t = 25.14, df = 22	<0.0001

S2D	Valproic Acid	1mg/kg_3-Chamber	7	7	7	7	3-way ANOVA		Drug x Sex	F (1, 24) = 0.1048	0.7489
			7	7	7	7	3-way ANOVA		Drug x Genotype	F (1, 24) = 0.001932	0.9653
			7	7	7	7	3-way ANOVA		Sex x Genotype	F (1, 24) = 0.01212	0.9132
			7	7	7	7	3-way ANOVA	Šídák's	Saline-CON-F vs Saline-ASD-F	t = 4.412, df = 48	0.0016
			7	7	7	7	3-way ANOVA	Šídák's	Saline-CON-M vs Saline-ASD-M	t = 4.658, df = 48	0.0007
		3mg/kg_3-Chamber	7	7	6	7	3-way ANOVA		Drug x Sex	F (1, 22) = 0.001859	0.966
			7	7	6	7	3-way ANOVA		Drug x Genotype	F (1, 22) = 2.432	0.1332
			7	7	6	7	3-way ANOVA		Sex x Genotype	F (1, 22) = 0.1253	0.7268
			7	7	6	7	3-way ANOVA	Šídák's	Saline-CON-F vs Saline-ASD-F	t = 5.613, df = 44	<0.0001
			7	7	6	7	3-way ANOVA	Šídák's	Saline-CON-M vs Saline-ASD-M	t = 5.529, df = 44	<0.0001
		10mg/kg_3-Chamber	7	7	7	7	3-way ANOVA		Drug x Sex	F (1, 24) = 0.1648	0.6884
			7	7	7	7	3-way ANOVA		Drug x Genotype	F (1, 24) = 55.89	<0.0001
			7	7	7	7	3-way ANOVA		Sex x Genotype	F (1, 24) = 0.03053	0.8628
			7	7	7	7	3-way ANOVA	Šídák's	Saline-CON-F vs Saline-ASD-F	t = 5.139, df = 48	0.0001
			7	7	7	7	3-way ANOVA	Šídák's	Saline-CON-M vs Saline-ASD-M	t = 5.604, df = 48	<0.0001
			7	7	7	7	3-way ANOVA	Šídák's	Saline-ASD-F vs Drug-ASD-F	t = 7.332, df = 24	<0.0001
			7	7	7	7	3-way ANOVA	Šídák's	Saline-ASD-M vs Drug-ASD-M	t = 7.314, df = 24	<0.0001
		30mg/kg_3-Chamber	7	7	6	7	3-way ANOVA		Drug x Sex	F (1, 22) = 0.003733	0.9518
			7	7	6	7	3-way ANOVA		Drug x Genotype	F (1, 22) = 13.56	0.0013
			7	7	6	7	3-way ANOVA		Sex x Genotype	F (1, 22) = 0.1680	0.6859
			7	7	6	7	3-way ANOVA	Šídák's	Saline-CON-F vs Saline-ASD-F	t = 3.997, df = 44	0.0067
7	7		6	7	3-way ANOVA	Šídák's	Saline-CON-M vs Saline-ASD-M	t = 4.274, df = 44	0.0028		
7	7		6	7	3-way ANOVA	Šídák's	Saline-ASD-F vs Drug-ASD-F	t = 5.346, df = 22	0.0006		
7	7		6	7	3-way ANOVA	Šídák's	Saline-ASD-M vs Drug-ASD-M	t = 6.423, df = 22	<0.0001		
S3B	<i>Cntnap2^{-/-}</i>	CPP	8	11	7	6	3-way ANOVA		Test x Sex	F (1, 28) = 0.3109	0.5815
			8	11	7	6	3-way ANOVA		Test x Genotype	F (1, 28) = 0.003460	0.9535
			8	11	7	6	3-way ANOVA		Sex x Genotype	F (1, 28) = 2.264	0.1436
S4A	<i>Sert-Cre^{+/+};16p11.2^{flx/flx}</i>	Locomotion	6	11	13	9	3-way ANOVA		Drug x Genotype	F (1, 35) = 0.3449	0.5608
			6	11	13	9	3-way ANOVA		Drug x Sex	F (1, 35) = 0.5986	0.4443
			6	11	13	9	3-way ANOVA		Sex x Genotype	F (1, 35) = 0.3268	0.5712
S4B	<i>Cntnap2^{-/-}</i>	Locomotion	9	14	9	9	3-way ANOVA		Drug x Genotype	F (1, 37) = 35.67	<0.0001
			9	14	9	9	3-way ANOVA		Drug x Sex	F (1, 37) = 0.01902	0.8911
			9	14	9	9	3-way ANOVA		Sex x Genotype	F (1, 37) = 0.1879	0.6672
			9	14	9	9	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 5.523, df = 37	<0.0001
			9	14	9	9	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 5.461, df = 37	<0.0001
S4C	<i>Fmr1^{-y,-/-}</i>	Locomotion	10	10	10	10	3-way ANOVA		Drug x Genotype	F (1, 36) = 33.42	<0.0001
			10	10	10	10	3-way ANOVA		Drug x Sex	F (1, 36) = 0.09303	0.7621
			10	10	10	10	3-way ANOVA		Sex x Genotype	F (1, 36) = 3.428	0.0723
			10	10	10	10	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 4.448, df = 36	0.001
			10	10	10	10	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 3.942, df = 36	0.0043
S4D	Valproic Acid	Locomotion	9	8	5	5	3-way ANOVA		Drug x Genotype	F (1, 23) = 6.353	0.0191
			9	8	5	5	3-way ANOVA		Drug x Sex	F (1, 23) = 0.09447	0.7613
			9	8	5	5	3-way ANOVA		Sex x Genotype	F (1, 23) = 6.134	0.021
			9	8	5	5	3-way ANOVA	Šídák's	saline:CON_M vs. saline:ASD-M	t = 3.03, df = 46	0.0469
S5A	<i>Sert-Cre^{+/+};16p11.2^{flx/flx}</i>	Novel Object	6	11	13	9	3-way ANOVA		Drug x Genotype	F (1, 35) = 0.1535	0.6976
			6	11	13	9	3-way ANOVA		Drug x Sex	F (1, 35) = 0.2561	0.616
			6	11	13	9	3-way ANOVA		Sex x Genotype	F (1, 35) = 0.1014	0.7521
S5B	<i>Cntnap2^{-/-}</i>	Novel Object	9	14	9	9	3-way ANOVA		Drug x Genotype	F (1, 37) = 0.03463	0.8534
			9	14	9	9	3-way ANOVA		Drug x Sex	F (1, 37) = 0.07164	0.7904
			9	14	9	9	3-way ANOVA		Sex x Genotype	F (1, 37) = 0.4193	0.5213
S5C	<i>Fmr1^{-y,-/-}</i>	Novel Object	10	10	10	10	3-way ANOVA		Drug x Genotype	F (1, 36) = 0.01115	0.9165
			10	10	10	10	3-way ANOVA		Drug x Sex	F (1, 36) = 0.03267	0.8576

			10	10	10	10	3-way ANOVA		Sex x Genotype	F (1, 36) = 0.8697	0.3572
S5D	Valproic Acid	Novel Object	9	8	5	5	3-way ANOVA		Drug x Genotype	F (1, 23) = 0.01465	0.9047
			9	8	5	5	3-way ANOVA		Drug x Sex	F (1, 23) = 0.6770	0.4191
			9	8	5	5	3-way ANOVA		Sex x Genotype	F (1, 23) = 0.2446	0.6256
			9	8	5	5	3-way ANOVA		Sex x Genotype	F (1, 23) = 0.2446	0.6256
S6A	<i>Act16b</i> ^{-/-}	Locomotion	7	7	7	9	3-way ANOVA		Drug x Genotype	F (1, 26) = 27.86	<0.0001
			7	7	7	9	3-way ANOVA		Drug x Sex	F (1, 26) = 1.371	0.2523
			7	7	7	9	3-way ANOVA		Sex x Genotype	F (1, 26) = 0.8843	0.3557
			7	7	7	9	3-way ANOVA	Šídák's	saline:ASD-F vs. drug:ASD-F	t = 4.213, df = 26	0.0032
			7	7	7	9	3-way ANOVA	Šídák's	saline:ASD-M vs. drug:ASD-M	t = 4.599, df = 26	0.0012
S6B	<i>Act16b</i> ^{-/-}	Novel Object	12	6	8	11	3-way ANOVA		Drug x Genotype	F (1, 33) = 0.4949	0.4867
			12	6	8	11	3-way ANOVA		Drug x Sex	F (1, 33) = 1.161	0.289
			12	6	8	11	3-way ANOVA		Sex x Genotype	F (1, 33) = 0.5300	0.4718
S7A	<i>Sert-Cre</i> ^{+/-} : <i>Arid1b</i> ^{flx/+}	Novel Object	14	12	10	5	2-way ANOVA		Interaction	F (1, 37) = 0.05852	0.8102
			14	12	10	5	2-way ANOVA		Genotype	F (1, 37) = 0.2552	0.6165
			14	12	10	5	2-way ANOVA		Sex	F (1, 37) = 0.1637	0.6881
		Locomotion	14	12	8	5	2-way ANOVA		Interaction	F (1, 35) = 2.108	0.1554
			14	12	8	5	2-way ANOVA		Genotype	F (1, 35) = 0.6073	0.441
			14	12	8	5	2-way ANOVA		Sex	F (1, 35) = 2.160	0.1506
S7B	<i>Sert-Cre</i> ^{+/-} : <i>Arid1b</i> ^{flx/+}	Novel Object	14	12	8	5	3-way ANOVA		Drug x Genotype	F (1, 35) = 0.1814	0.6728
			14	12	8	5	3-way ANOVA		Drug x Sex	F (1, 35) = 1.002	0.3238
			14	12	8	5	3-way ANOVA		Sex x Genotype	F (1, 35) = 1.128	0.2954
		Locomotion	14	12	8	5	3-way ANOVA		Drug x Genotype	F (1, 35) = 0.2839	0.5975
			14	12	8	5	3-way ANOVA		Drug x Sex	F (1, 35) = 0.0001173	0.9914
			14	12	8	5	3-way ANOVA		Sex x Genotype	F (1, 35) = 1.315	0.2593

Table S3: Principal Component Analysis Loading Tables**Fig. 5A**

	PC1	PC2	PC3	PC4
Juvenile interaction	0.3939387	-0.72915424	0.1868903	0.5274641
Novel object	0.4076447	0.66436628	0.4193884	0.4653565
3-chamber	0.4992497	0.14169781	-0.8459347	0.1227434
Open field	0.6552769	-0.08290525	0.2712561	-0.7001135
Proportion of variance explained	0.3903	0.2729	0.2029	0.1338

Fig. 5B

	PC1	PC2	PC3	PC4
Juvenile interaction	-0.6109104	0.2732012	0.27931587	-0.68857259
Novel object	0.2730455	0.7612845	-0.56339974	-0.16873895
3-chamber	-0.5903668	0.3993712	0.04386828	0.70003229
Open field	0.4513332	0.4316360	0.77629824	0.08573066
Proportion of variance explained	0.4544	0.2717	0.1761	0.09785

Fig.5C

	PC1	PC2	PC3	PC4
Juvenile interaction	-0.3491435	-0.75148372	0.1285818	0.54482815
Novel object	0.7317828	0.05452042	-0.2924698	0.61317449
3-chamber	-0.3338837	-0.03965004	-0.9406233	-0.04666176
Open field	0.4807436	-0.65629842	-0.1146993	-0.57008947
Proportion of variance explained	0.328	0.2908	0.2404	0.1409

Fig.5D-E

	PC1	PC2	PC3	PC4
Juvenile interaction	-0.5817174	0.3637999	0.3533411	-0.6359281
Novel object	0.3726226	0.6552791	-0.5882299	-0.2928262
3-chamber	-0.5750399	0.4361641	-0.2071580	0.6604358
Open field	0.4382766	0.4980158	0.6972956	0.2714272
Proportion of variance explained	0.4175	0.2655	0.1954	0.1216

These tables show the correlation between each of the principal components and each of the original variables, as well as the variance explained by each principal component.