

# Supplementary information for

## Sustained effects of rapidly-acting antidepressants require BDNF-dependent MeCP2 phosphorylation

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### **This supplementary information includes:**

Supplementary Table 1

Supplementary Table 1

Fig. 1b

	Time	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
BDNF/GAPDH	30 min	Sal	8	1.0 ± 0.05861	Unpaired t-test	$t_{(13)} = 2.680$ $P = 0.0189 / *$
		Ket	7	1.326 ± 0.1119		
	7 days	Sal	9	1.0 ± 0.1363	Unpaired t-test	$t_{(16)} = 0.5541$ $P = 0.5872 / \text{N.S.}$
		Ket	9	1.106 ± 0.1329		
pMeCP2/MeCP2	30 min	Sal	8	1.0 ± 0.09987	Unpaired t-test	$t_{(14)} = 0.3760$ $P = 0.7126 / \text{N.S.}$
		Ket	8	1.075 ± 0.1727		
	7 days	Sal	9	1.0 ± 0.1381	Unpaired t-test	$t_{(18)} = 2.765$ $P = 0.0127 / *$
		Ket	11	1.730 ± 0.2098		

Fig. 1c

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	10	177.5 ± 10.38	Two-way ANOVA	$F_{(1, 41)} = 1.170$ $P = 0.2857$	$F_{(1, 41)} = 0.1077$ $P = 0.7445$	$F_{(1, 41)} = 23.14$ $P < 0.0001$	CTL: Sal vs Ket
	Ket	10	96.00 ± 20.40					$P = 0.0016 / **$
<i>Mecp2</i> KI	Sal	13	167.1 ± 9.839					KI: Sal vs Ket
	Ket	12	115.5 ± 13.72					$P = 0.0378 / *$

Fig. 1d

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	9	193.3 ± 7.448	Two-way ANOVA	$F_{(1, 31)} = 5.798$ $P = 0.0222$	$F_{(1, 31)} = 2.499$ $P = 0.1241$	$F_{(1, 31)} = 4.502$ $P = 0.0420$	CTL: Sal vs Ket
	Ket	9	143.4 ± 17.71					$P = 0.0139 / *$
<i>Mecp2</i> KI	Sal	9	184.2 ± 6.702					KI: Sal vs Ket
	Ket	8	187.4 ± 7.329					$P = 0.9971 / \text{N.S.}$

Fig. 1e

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	13	1.0 ± 0.0994	Two-way ANOVA	$F_{(1, 45)} = 4.192$ $P = 0.0465$	$F_{(1, 45)} = 8.757$ $P = 0.0049$	$F_{(1, 45)} = 3.562$ $P = 0.0656$	CTL: Sal vs Ket
	Ket	13	1.459 ± 0.1414					$P = 0.0303 / *$
<i>Bdnf</i> cKO	Sal	11	0.8936 ± 0.0996					cKO: Sal vs Ket
	Ket	12	0.8749 ± 0.1142					$P = 0.9995 / \text{N.S.}$

**Fig. 1f**

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	12	196.4 ± 6.427	Two-way ANOVA	$F_{(1,36)} = 4.290$ $P = 0.0456$	$F_{(1,36)} = 0.2076$ $P = 0.6514$	$F_{(1,36)} = 6.008$ $P = 0.0192$	CTL: Sal vs Ket $P = 0.0054 / **$
	Ket	12	135.4 ± 15.59					
<i>Bdnf</i> cKO	Sal	8	174.6 ± 20.43					
	Ket	8	169.5 ± 5.913					

**Fig. 2a**

Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
ActD-Sal	10	154.8 ± 10.87	Unpaired t-test	$t_{(17)} = 0.7179$ $P = 0.4826 / N.S.$
ActD-Ket	9	165.4 ± 9.905		

**Fig. 2b**

Time	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
30 min	Sal	8	1.0 ± 0.2228	Unpaired t-test	$t_{(14)} = 1.039$ $P = 0.3165 / N.S.$
	Ket	8	1.345 ± 0.2458		
7 days	Sal	9	1.0 ± 0.2587	Unpaired t-test	$t_{(16)} = 0.6954$ $P = 0.4968 / N.S.$
	Ket	9	0.7823 ± 0.1763		

**Fig. 2c**

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	9	137.7 ± 6.384	Two-way ANOVA	$F_{(1,27)} = 1.954$ $P = 0.1735$	$F_{(1,27)} = 6.927$ $P = 0.0139$	$F_{(1,27)} = 33.39$ $P < 0.0001$	CTL-Sal vs CTL-Ket $P < 0.0001 / ***$
	Ket	8	73.89 ± 10.46					
<i>Mef2c</i> cKO	Sal	7	101.9 ± 9.388					
	Ket	7	62.91 ± 9.271					

**Fig. 2d**

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	9	144.6 ± 7.23	Two-way ANOVA	$F_{(1,27)} = 0.0015$ $P = 0.9693$	$F_{(1,27)} = 0.0913$ $P = 0.7649$	$F_{(1,27)} = 100.7$ $P < 0.0001$	CTL-Sal vs CTL-Ket $P < 0.0001 / ***$
	Ket	8	61.86 ± 6.518					
<i>Mef2c</i> cKO	Sal	7	141.8 ± 10.88					
	Ket	7	59.7 ± 8.228					

**Fig. 3b-c**

Pre-treatment	Perfusion	N number	Mean ±S.E.M	Statistics	P-value /Significance
Sal(i.p.)	ACSF	6	96.93 ± 2.701	Unpaired t-test	Sal-ACSF vs Sal-Ket $t_{(15)} = 5.683, P < 0.0001 / ***$
	Ket	11	116 ± 1.994		Ket-ACSF vs Ket-Ket $t_{(16)} = 3.722, P = 0.0019 / **$
Ket (i.p.)	ACSF	8	96.04 ± 1.783		Sal-Ket vs Ket-Ket $t_{(19)} = 2.404, P = 0.0266 / *$
	Ket	10	140.7 ± 10.57		

**Fig. 3d-e**

Pre-treatment	Perfusion	N number	Mean ±S.E.M	Statistics	P-value /Significance
Sal(i.p.)	ACSF	7	96.64 ± 3.632	Unpaired t-test	Sal-ACSF vs Sal-Ket $t_{(12)} = 4.034, P = 0.0017 / **$
	Ket	7	118.7 ± 4.103		Ket-ACSF vs Ket-Ket $t_{(15)} = 3.802, P = 0.0017 / **$
Ket (i.p.)	ACSF	8	95.84 ± 1.877		Sal-Ket vs Ket-Ket $t_{(14)} = 0.3591, P = 0.7249 / N.S.$
	Ket	9	121.6 ± 6.139		

**Fig. 4a**

Time	Group	N number	Mean ±S.E.M	Statistics	Interaction	Time factor	Drug factor	P-value /Significance
8 hr	Sal	9	149.4 ± 7.932	Two-way ANOVA	$F_{(1, 30)} = 0.054$ $P = 0.8182$	$F_{(1, 30)} = 1.003$ $P = 0.3245$	$F_{(1, 30)} = 17.61$ $P = 0.0002$	8 hr: Sal vs SCA $P = 0.0151 / *$
	SCA	9	112.4 ± 7.565					24 hr: Sal vs SCA $P = 0.0494 / *$
24 hr	Sal	8	155.9 ± 8.501					
	SCA	8	122.8 ± 9.486					

**Fig. 4b**

Experiment	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
PCR (mRNA)	30 min: Sal	6	1.0 ± 0.0675	Unpaired t-test	$t_{(10)} = 0.8081$ $P = 0.4378 / N.S.$
	30 min: SCA	6	0.9306 ± 0.0531		
	8 hrs: Sal	7	1.0 ± 0.0201	Unpaired t-test	$t_{(12)} = 2.067$ $P = 0.0305 / *$
	8 hrs: SCA	7	1.683 ± 0.0262		
	24 hrs: Sal	8	1.0 ± 0.0966	Unpaired t-test	$t_{(14)} = 0.1246$ $P = 0.9026 / N.S.$
	24 hrs: SCA	8	1.021 ± 0.1396		
Western blot (protein)	30 min: Sal	6	1.0 ± 0.1068	Unpaired t-test	$t_{(10)} = 0.6783$ $P = 0.5130 / N.S.$
	30 min: SCA	6	0.9168 ± 0.0604		
	8 hrs: Sal	15	1.0 ± 0.1009	Unpaired t-test	$t_{(28)} = 1.777$ $P = 0.0865 / N.S.$
	8 hrs: SCA	15	1.240 ± 0.0901		
	24 hrs: Sal	8	1.0 ± 0.1070	Unpaired t-test	$t_{(14)} = 0.6677$ $P = 0.5152 / N.S.$
	24 hrs: SCA	8	0.8708 ± 0.1612		

**Fig. 4c**

Time	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
8 h	Sal	8	1.0 ± 0.1368	Unpaired t-test	$t_{(14)} = 0.7534$ $P = 0.4637 / N.S.$
	SCA	8	0.8718 ± 0.1011		
24 h	Sal	7	1.0 ± 0.1335	Welch's correction	$t_{(2,313)} = 8.884$ $P = 0.0464 / *$
	SCA	8	1.883 ± 0.3577		

**Fig. 4d**

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	10	1.0 ± 0.1143	Two-way ANOVA	$F_{(1, 40)} = 5.760$ $P = 0.0211$	$F_{(1, 40)} = 0.3670$ $P = 0.5481$	$F_{(1, 40)} = 3.870$ $P = 0.0581$	CTL: Sal vs SCA $P = 0.0045 / **$
	SCA	12	1.735 ± 0.1993					cKO: Sal vs SCA $P = 0.7470 / N.S.$
<i>Bdnf</i> cKO	Sal	11	1.303 ± 0.1940					
	SCA	11	1.227 ± 0.1348					

Fig. 4e

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	16	181.3 ± 9.904	Two-way ANOVA	$F_{(1, 54)} = 8.356$ $P = 0.0055$	$F_{(1, 54)} = 17.85$ $P < 0.0001$	$F_{(1, 54)} = 15.49$ $P = 0.0002$	CTL: Sal vs SCA $P < 0.0001$ / ***
	SCA	14	196.9 ± 6.220					cKO: Sal vs SCA $P = 0.8908$ / N.S.
<i>Bdnf</i> cKO	Sal	15	101.4 ± 17.65					
	SCA	13	184.7 ± 8.262					

Fig. 4f

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	17	159.4 ± 10.53	two-way ANOVA	$F_{(1, 61)} = 4.183$ $P = 0.0451$	$F_{(1, 61)} = 1.454$ $P = 0.2325$	$F_{(1, 61)} = 3.206$ $P = 0.0783$	CTL: Sal vs SCA $P = 0.0315$ / *
	SCA	18	118.6 ± 11.53					cKO: Sal vs SCA $P = 0.9981$ / N.S.
<i>Bdnf</i> cKO	Sal	16	150.4 ± 11.17					
	SCA	14	153.1 ± 7.438					

Fig. 4g

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	13	173.2 ± 7.548	two-way ANOVA	$F_{(1, 53)} = 1.295$ $P = 0.2602$	$F_{(1, 53)} = 2.425$ $P = 0.1254$	$F_{(1, 53)} = 39.04$ $P < 0.0001$	CTL: Sal vs SCA $P = 0.0048$ / **
	SCA	16	118.7 ± 9.749					KI: Sal vs SCA $P < 0.0001$ / ***
<i>MeCP2</i> KI	Sal	14	168.7 ± 8.802					
	SCA	14	90 ± 14.91					

Fig. 4h

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance
CTL	Sal	9	187.8 ± 5.174	two-way ANOVA	$F_{(1, 35)} = 6.09$ $P = 0.0186$	$F_{(1, 35)} = 0.2507$ $P = 0.6197$	$F_{(1, 35)} = 2.359$ $P = 0.1335$	CTL: Sal vs SCA $P = 0.0340$ / *
	SCA	11	143.0 ± 8.348					KI: Sal vs SCA $P = 0.9142$ / N.S.
<i>MeCP2</i> KI	Sal	9	165.8 ± 19.54					
	SCA	10	176.2 ± 7.669					

**Fig. 5a**

Time point	N number	Mean ±S.E.M	Statistics	P-value /Significance
Base	8	100	Paired t-test	$t_{(7)} = 0.5035, P = 0.6301 / \text{N.S.}$
SCA		98.23 ± 3.516		

**Fig. 5b**

Time point	N number	Mean ±S.E.M	Statistics	P-value /Significance
Base	7	100	Paired t-test	$t_{(6)} = 11.81, P < 0.0001 / \text{***}$
Washout (LTD)		72.50 ± 2.329		

**Fig. 5c**

Time point	N number	Mean ±S.E.M	One-Way RM ANOVA	Post-hoc test	P-value /Significance
Base	11	100	$F_{(2, 20)} = 25.11,$ $P < 0.0001$		
Wash1 (LTD)		73.82 ± 3.412		Base vs Wash1	$P < 0.0001 / \text{***}$
Wash2		86.87 ± 3.279		Wash1 vs Wash2	$P = 0.0057 / \text{**}$

**Fig.5d**

Interstimulus interval	Timepoint	N number	Mean ±S.E.M	Statistics	P-value /Significance
20	Before	8	1.329 ± 0.08022	Paired t-test	$t_{(7)} = 0.6319, P = 0.5475 / \text{N.S.}$
	After	8	1.348 ± 0.07643		
30	Before	8	1.421 ± 0.08378	Paired t-test	$t_{(7)} = 0.7230, P = 0.4931 / \text{N.S.}$
	After	8	1.401 ± 0.06265		
50	Before	8	1.430 ± 0.07573	Paired t-test	$t_{(7)} = 0.0124, P = 0.9904 / \text{N.S.}$
	After	8	1.429 ± 0.05855		
100	Before	8	1.413 ± 0.05774	Paired t-test	$t_{(7)} = 0.4682, P = 0.6539 / \text{N.S.}$
	After	8	1.435 ± 0.06459		
200	Before	8	1.232 ± 0.03728	Paired t-test	$t_{(7)} = 1.747, P = 0.2058 / \text{N.S.}$
	After	8	1.212 ± 0.03748		
400	Before	8	1.051 ± 0.02456	Paired t-test	$t_{(7)} = 1.395, P = 0.1241 / \text{N.S.}$
	After	8	1.101 ± 0.02040		
500	Before	8	1.058 ± 0.02827	Paired t-test	$t_{(7)} = 0.2232, P = 0.8297 / \text{N.S.}$
	After	8	1.063 ± 0.02224		

**Fig.5e**

<b>Interstimulus interval</b>	<b>Timepoint</b>	<b>N number</b>	<b>Mean ±S.E.M</b>	<b>Statistics</b>	<b>P-value /Significance</b>
20	Before	7	1.376 ± 0.04804	Paired t-test	$t_{(6)} = 5.441, P = 0.0016 / **$
	After	7	1.524 ± 0.05865		
30	Before	7	1.406 ± 0.02681	Paired t-test	$t_{(6)} = 3.131, P = 0.0203 / *$
	After	7	1.541 ± 0.04391		
50	Before	7	1.413 ± 0.03502	Paired t-test	$t_{(6)} = 3.239, P = 0.0177 / *$
	After	7	1.539 ± 0.03877		
100	Before	7	1.480 ± 0.05091	Paired t-test	$t_{(6)} = 2.510, P = 0.0459 / *$
	After	7	1.602 ± 0.06754		
200	Before	7	1.276 ± 0.04418	Paired t-test	$t_{(6)} = 0.6406, P = 0.5454 / \text{N.S.}$
	After	7	1.294 ± 0.05554		
400	Before	7	1.113 ± 0.03046	Paired t-test	$t_{(6)} = 0.0197, P = 0.9849 / \text{N.S.}$
	After	7	1.112 ± 0.06050		
500	Before	7	1.070 ± 0.03428	Paired t-test	$t_{(6)} = 0.2255, P = 0.8291 / \text{N.S.}$
	After	7	1.056 ± 0.03106		



**Fig.5f**

<b>Interstimulus interval</b>	<b>Group</b>	<b>N number</b>	<b>Mean ±S.E.M</b>	<b>One-way RM ANOVA</b>	<b>Comparison</b>	<b>P-value /Significance</b>
20	Base	11	1.238 ± 0.04585	$F_{(3, 30)} = 3.461,$ $P = 0.0285$	Base vs Physo	$P = 0.0172 / *$
	Physo	11	1.387 ± 0.05012		Physo vs SCA	$P = 0.3637 / \text{N.S.}$
	SCA	11	1.309 ± 0.06031		Physo vs Wash2	$P = 0.1915 / \text{N.S.}$
	Wash2	11	1.290 ± 0.04420		SCA vs Wash2	$P = 0.9784 / \text{N.S.}$
30	Base	11	1.415 ± 0.04579	$F_{(3, 30)} = 7.876,$ $P = 0.0005$	Base vs Physo	$P = 0.0024 / **$
	Physo	11	1.670 ± 0.09548		Physo vs SCA	$P = 0.0007 / ***$
	SCA	11	1.385 ± 0.03716		Physo vs Wash2	$P = 0.0216 / *$
	Wash2	11	1.471 ± 0.06552		SCA vs Wash2	$P = 0.5525 / \text{N.S.}$
50	Base	11	1.454 ± 0.03419	$F_{(3, 30)} = 8.660,$ $P = 0.0003$	Base vs Physo	$P = 0.0024 / **$
	Physo	11	1.639 ± 0.05900		Physo vs SCA	$P = 0.0025 / **$
	SCA	11	1.455 ± 0.05756		Physo vs Wash2	$P = 0.0005 / ***$
	Wash2	11	1.427 ± 0.04083		SCA vs Wash2	$P = 0.934 / \text{N.S.}$
100	Base	11	1.441 ± 0.04462	$F_{(3, 30)} = 3.315,$ $P = 0.0331$	Base vs Physo	$P = 0.0113 / *$
	Physo	11	1.581 ± 0.04669		Physo vs SCA	$P = 0.0195 / *$
	SCA	11	1.453 ± 0.05180		Physo vs Wash2	$P = 0.0166 / *$
	Wash2	11	1.450 ± 0.04027		SCA vs Wash2	$P = 0.9454 / \text{N.S.}$
200	Base	11	1.259 ± 0.03321	$F_{(3, 30)} = 2.126,$ $P = 0.1177$	Base vs Physo	$P = 0.3111 / \text{N.S.}$
	Physo	11	1.334 ± 0.02888		Physo vs SCA	$P = 0.2798 / \text{N.S.}$
	SCA	11	1.257 ± 0.03446		Physo vs Wash2	$P = 0.9999 / \text{N.S.}$
	Wash2	11	1.333 ± 0.05002		SCA vs Wash2	$P = 0.2892 / \text{N.S.}$
400	Base	11	1.078 ± 0.01582	$F_{(3, 30)} = 1.403,$ $P = 0.2610$	Base vs Physo	$P = 0.9968 / \text{N.S.}$
	Physo	11	1.07 ± 0.03115		Physo vs SCA	$P = 0.3929 / \text{N.S.}$
	SCA	11	1.132 ± 0.04141		Physo vs Wash2	$P = 0.9920 / \text{N.S.}$
	Wash2	11	1.059 ± 0.02365		SCA vs Wash2	$P = 0.2564 / \text{N.S.}$
500	Base	11	1.059 ± 0.01987	$F_{(3, 30)} = 0.5066,$ $P = 0.6807$	Base vs Physo	$P = 0.9998 / \text{N.S.}$
	Physo	11	1.055 ± 0.03727		Physo vs SCA	$P = 0.6955 / \text{N.S.}$
	SCA	11	1.114 ± 0.06278		Physo vs Wash2	$P = 0.9936 / \text{N.S.}$
	Wash2	11	1.069 ± 0.02764		SCA vs Wash2	$P = 0.8381 / \text{N.S.}$

Fig.5g

Interstimulus interval	Group	N number	Mean ±S.E.M	One-way ANOVA	Post-hoc test	P-value /Significance
20	Sal	20	1.433 ± 0.0307	$F_{(2, 61)} = 4.349,$ $P = 0.0171$		
	SCA (8 h)	24	1.299 ± 0.0441		Sal vs SCA (8 h)	$P = 0.0231 / *$
	SCA (24 h)	20	1.294 ± 0.0304		Sal vs SCA (24 h)	$P = 0.0238 / *$
30	Sal	20	1.494 ± 0.0403	$F_{(2, 61)} = 3.561,$ $P = 0.0345$		
	SCA (8 h)	24	1.394 ± 0.0274		Sal vs SCA (8 h)	$P = 0.0465 / *$
	SCA (24 h)	20	1.386 ± 0.0251		Sal vs SCA (24 h)	$P = 0.0394 / *$
50	Sal	20	1.546 ± 0.0273	$F_{(2, 61)} = 5.169,$ $P = 0.0084$		
	SCA (8 h)	24	1.413 ± 0.0342		Sal vs SCA (8 h)	$P = 0.0054 / **$
	SCA (24 h)	20	1.443 ± 0.0271		Sal vs SCA (24 h)	$P = 0.0455 / *$
100	Sal	20	1.426 ± 0.0236	$F_{(2, 61)} = 0.7896,$ $P = 0.4586$		
	SCA (8 h)	24	1.391 ± 0.0281		Sal vs SCA (8 h)	$P = 0.5605 / N.S.$
	SCA (24 h)	20	1.377 ± 0.0306		Sal vs SCA (24 h)	$P = 0.3742 / N.S.$
200	Sal	20	1.230 ± 0.0226	$F_{(2, 61)} = 0.5068,$ $P = 0.6049$		
	SCA (8 h)	24	1.197 ± 0.0261		Sal vs SCA (8 h)	$P = 0.5816 / N.S.$
	SCA (24 h)	20	1.196 ± 0.0306		Sal vs SCA (24 h)	$P = 0.5851 / N.S.$
400	Sal	20	1.086 ± 0.0219	$F_{(2, 61)} = 5.716,$ $P = 0.0053$		
	SCA (8 h)	24	1.018 ± 0.0099		Sal vs SCA (8 h)	$P = 0.0186 / *$
	SCA (24 h)	20	1.097 ± 0.0234		Sal vs SCA (24 h)	$P = 0.8968 / N.S.$
500	Sal	20	1.067 ± 0.0237	$F_{(2, 61)} = 0.9880,$ $P = 0.3782$		
	SCA (8 h)	24	1.029 ± 0.0163		Sal vs SCA (8 h)	$P = 0.2767 / N.S.$
	SCA (24 h)	20	1.046 ± 0.0179		Sal vs SCA (24 h)	$P = 0.6880 / N.S.$

**Fig. 5h**

Genotype	Interstimulus interval	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance		
CTL	20	Sal	20	1.342 ± 0.0274	Unpaired t-test	$t_{(38)} = 3.666, P = 0.0008 / ***$		
		SCA (24 h)	20	1.204 ± 0.0261				
	30	Sal	20	1.414 ± 0.0374	Unpaired t-test	$t_{(38)} = 2.756, P = 0.0089 / **$		
		SCA (24 h)	20	1.293 ± 0.0230				
	50	Sal	20	1.474 ± 0.0273	Unpaired t-test	$t_{(38)} = 3.745, P = 0.0006 / ***$		
		SCA (24 h)	20	1.351 ± 0.0186				
	100	Sal	20	1.406 ± 0.0282	Unpaired t-test	$t_{(38)} = 2.225, P = 0.0321 / *$		
		SCA (24 h)	20	1.327 ± 0.0212				
	200	Sal	20	1.197 ± 0.0208	Mann-Whitney test	$U = 157, P = 0.2534 / N.S.$		
		SCA (24 h)	20	1.171 ± 0.0126				
	400	Sal	20	1.070 ± 0.0181	Unpaired t-test	$t_{(38)} = 0.1855, P = 0.8538 / N.S.$		
		SCA (24 h)	20	1.067 ± 0.0103				
	500	Sal	20	1.071 ± 0.0169	Unpaired t-test	$t_{(38)} = 2.0333, P = 0.0491 / *$		
		SCA (24 h)	20	1.023 ± 0.0163				
Mecp2 KI	20	Sal	17	1.357 ± 0.0354	One-way ANOVA			
		SCA (8 h)	15	1.242 ± 0.218				
		SCA (24 h)	14	1.453 ± 0.0446				
	30	Sal	17	1.427 ± 0.0439	One-way ANOVA			
		SCA (8 h)	15	1.328 ± 0.0125				
		SCA (24 h)	14	1.495 ± 0.05918				
	50	Sal	17	1.517 ± 0.0393	One-way ANOVA			
		SCA (8 h)	15	1.376 ± 0.0230				
		SCA (24 h)	14	1.527 ± 0.0531				
	100	Sal	17	1.382 ± 0.0432	One-way ANOVA			
		SCA (8 h)	15	1.362 ± 0.0235				
		SCA (24 h)	14	1.474 ± 0.0415				
	200	Sal	17	1.216 ± 0.0281	One-way ANOVA			
		SCA (8 h)	15	1.195 ± 0.0200				
		SCA (24 h)	14	1.222 ± 0.0244				
	400	Sal	17	1.098 ± 0.0225	One-way ANOVA			
		SCA (8 h)	15	1.098 ± 0.0175				
		SCA (24 h)	14	1.077 ± 0.0157				
	500	Sal	17	1.092 ± 0.0227	One-way ANOVA			
		SCA (8 h)	15	1.040 ± 0.0178				
		SCA (24 h)	14	1.090 ± 0.0247				
						$F_{(2, 43)} = 8.761,$	Sal vs SCA (8 h)	$P = 0.0392 / *$
						$P = 0.0006$	Sal vs SCA (24 h)	$P = 0.1059 / N.S.$
						$F_{(2, 43)} = 3.689,$	Sal vs SCA (8 h)	$P = 0.0427 / *$
					$P = 0.0332$	Sal vs SCA (24 h)	$P = 0.3593 / N.S.$	
					$F_{(2, 43)} = 4.407,$	Sal vs SCA (8 h)	$P = 0.0271 / *$	
					$P = 0.0182$	Sal vs SCA (24 h)	$P = 0.8823 / N.S.$	
					$F_{(2, 43)} = 8.761,$	Sal vs SCA (8 h)	$P = 0.9004 / N.S.$	
					$P = 0.0006$	Sal vs SCA (24 h)	$P = 0.1639 / N.S.$	
					$F_{(2, 43)} = 0.3085,$	Sal vs SCA (8 h)	$P = 0.7805 / N.S.$	
					$P = 0.7361$	Sal vs SCA (24 h)	$P = 0.9772 / N.S.$	
					$F_{(2, 43)} = 0.3679,$	Sal vs SCA (8 h)	$P = 0.9997 / N.S.$	
					$P = 0.6943$	Sal vs SCA (24 h)	$P = 0.6776 / N.S.$	
					$F_{(2, 43)} = 1.777,$	Sal vs SCA (8 h)	$P = 0.1704 / N.S.$	
					$P = 0.1814$	Sal vs SCA (24 h)	$P = 0.9974 / N.S.$	

**Fig. 5i**

Genotype	Interstimulus interval	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance			
CTL	20	Sal	31	1.399 ± 0.0397	Unpaired t-test	$t_{(56)} = 2.675, P = 0.0098 / **$			
		SCA (24 h)	27	1.251 ± 0.0381					
	30	Sal	31	1.476 ± 0.326	Unpaired t-test	$t_{(56)} = 2.364, P = 0.0216 / *$			
		SCA (24 h)	27	1.366 ± 0.0336					
	50	Sal	31	1.521 ± 0.341	Welch's correction	$t_{(49.78)} = 2.706, P = 0.0093 / **$			
		SCA (24 h)	27	1.411 ± 0.0217					
	100	Sal	31	1.421 ± 0.0242	Unpaired t-test	$t_{(56)} = 0.7216, P = 0.4753 / \text{N.S.}$			
		SCA (24 h)	27	1.395 ± 0.0271					
	200	Sal	31	1.267 ± 0.0203	Unpaired t-test	$t_{(56)} = 2.491, P = 0.0157 / *$			
		SCA (24 h)	27	1.184 ± 0.0273					
	400	Sal	31	1.119 ± 0.0217	Mann-Whitney test	$U = 216, P = 0.0013 / **$			
		SCA (24 h)	27	1.031 ± 0.0152					
	500	Sal	31	1.078 ± 0.0192	Unpaired t-test	$t_{(56)} = 2.065, P = 0.0436 / *$			
		SCA (24 h)	27	1.015 ± 0.0239					
<i>Bdnf</i> cKO	20	Sal	21	1.375 ± 0.0487	One-way ANOVA				
		SCA (8 h)	11	1.370 ± 0.0448	$F_{(2, 55)} = 0.0165,$ $P = 0.9837$			Sal vs SCA (8 h)	$P = 0.9960 / \text{N.S.}$
		SCA (24 h)	26	1.381 ± 0.0325				Sal vs SCA (24 h)	$P = 0.9906 / \text{N.S.}$
	30	Sal	21	1.485 ± 0.0335	One-way ANOVA				
		SCA (8 h)	11	1.463 ± 0.0469	$F_{(2, 55)} = 0.0642,$ $P = 0.9379$			Sal vs SCA (8 h)	$P = 0.9208 / \text{N.S.}$
		SCA (24 h)	26	1.472 ± 0.0383				Sal vs SCA (24 h)	$P = 0.9549 / \text{N.S.}$
	50	Sal	21	1.488 ± 0.0382	One-way ANOVA				
		SCA (8 h)	11	1.498 ± 0.0451	$F_{(2, 55)} = 0.1163,$ $P = 0.8905$			Sal vs SCA (8 h)	$P = 0.9803 / \text{N.S.}$
		SCA (24 h)	26	1.473 ± 0.0259				Sal vs SCA (24 h)	$P = 0.9248 / \text{N.S.}$
	100	Sal	21	1.382 ± 0.0390	One-way ANOVA				
		SCA (8 h)	11	1.4 ± 0.0312	$F_{(2, 55)} = 0.2140,$ $P = 0.8080$			Sal vs SCA (8 h)	$P = 0.9405 / \text{N.S.}$
		SCA (24 h)	26	1.413 ± 0.0307				Sal vs SCA (24 h)	$P = 0.7453 / \text{N.S.}$
	200	Sal	21	1.185 ± 0.0284	One-way ANOVA				
		SCA (8 h)	11	1.214 ± 0.0250	$F_{(2, 55)} = 0.7722,$ $P = 0.4670$			Sal vs SCA (8 h)	$P = 0.7317 / \text{N.S.}$
		SCA (24 h)	26	1.227 ± 0.0221				Sal vs SCA (24 h)	$P = 0.3732 / \text{N.S.}$
	400	Sal	21	1.069 ± 0.0215	One-way ANOVA				
		SCA (8 h)	11	1.079 ± 0.0270	$F_{(2, 55)} = 0.0407,$ $P = 0.9602$			Sal vs SCA (8 h)	$P = 0.9455 / \text{N.S.}$
		SCA (24 h)	26	1.071 ± 0.0182				Sal vs SCA (24 h)	$P = 0.9949 / \text{N.S.}$
	500	Sal	21	1.047 ± 0.0286	One-way ANOVA				
		SCA (8 h)	11	1.049 ± 0.0242	$F_{(2, 55)} = 0.0165,$ $P = 0.9837$			Sal vs SCA (8 h)	$P = 0.9977 / \text{N.S.}$
		SCA (24 h)	26	1.061 ± 0.0175				Sal vs SCA (24 h)	$P = 0.8566 / \text{N.S.}$

**Fig. 6a**

Protein	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
pMeCP2/MeCP2	Sal	7	1.0 ± 0.2257	Unpaired t-test	$t_{(12)} = 2.465, P = 0.0298 / *$
	PRZP	7	1.647 ± 0.1338		
pCREB/CREB	Sal	8	1.0 ± 0.0278	Unpaired t-test	$t_{(13)} = 0.9481, P = 0.3604 / \text{N.S.}$
	PRZP	7	1.039 ± 0.0311		

**Fig. 6b**

Interstimulus interval	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
20	Sal	20	1.367 ± 0.0384	Unpaired t-test	$t_{(46)} = 2.545, P = 0.0143 / *$
	PRZP	28	1.226 ± 0.0380		
30	Sal	20	1.422 ± 0.0334	Unpaired t-test	$t_{(46)} = 3.509, P = 0.0010 / **$
	PRZP	28	1.27 ± 0.0278		
50	Sal	20	1.453 ± 0.0271	Unpaired t-test	$t_{(46)} = 2.201, P = 0.0328 / *$
	PRZP	28	1.363 ± 0.0287		
100	Sal	20	1.414 ± 0.0277	Unpaired t-test	$t_{(46)} = 2.196, P = 0.0331 / *$
	PRZP	28	1.334 ± 0.0236		
200	Sal	20	1.206 ± 0.0261	Mann-Whitney test	$U = 263, P = 0.7325 / \text{N.S.}$
	PRZP	28	1.207 ± 0.0174		
400	Sal	20	1.101 ± 0.0242	Unpaired t-test	$t_{(46)} = 0.9611, P = 0.3415 / \text{N.S.}$
	PRZP	28	1.075 ± 0.0156		
500	Sal	20	1.11 ± 0.0229	Mann-Whitney test	$U = 198, P = 0.0884 / \text{N.S.}$
	PRZP	28	1.068 ± 0.0156		

Fig. 6c

Interstimulus interval	Group	N number	Mean $\pm$ S.E.M	Statistics	Interaction	Drug factor	Genotype factor	P-value /Significance
20	CTL-Sal	18	1.421 $\pm$ 0.0450	Two-way ANOVA	$F_{(1, 67)} = 8.467$ $P = 0.0049$	$F_{(1, 67)} = 2.982$ $P = 0.0888$	$F_{(1, 67)} = 2.461$ $P = 0.1214$	CTL-Sal vs CTL-PRZP $P = 0.0082$ / **
	CTL-PRZP	18	1.217 $\pm$ 0.0326					KI-Sal vs KI-PRZP $P = 0.8398$ / N.S.
	KI-Sal	16	1.38 $\pm$ 0.0518					
	KI-PRZP	18	1.414 $\pm$ 0.0457					
30	CTL-Sal	18	1.482 $\pm$ 0.0400	Two-way ANOVA	$F_{(1, 67)} = 7.78$ $P = 0.0069$	$F_{(1, 67)} = 1.455$ $P = 0.2320$	$F_{(1, 67)} = 3.143$ $P = 0.0808$	CTL-Sal vs CTL-PRZP $P = 0.0293$ / *
	CTL-PRZP	18	1.33 $\pm$ 0.0265					KI-Sal vs KI-PRZP $P = 0.6838$ / N.S.
	KI-Sal	16	1.456 $\pm$ 0.0457					
	KI-PRZP	18	1.504 $\pm$ 0.0393					
50	CTL-Sal	18	1.514 $\pm$ 0.0303	Two-way ANOVA	$F_{(1, 67)} = 7.389$ $P = 0.0083$	$F_{(1, 67)} = 3.446$ $P = 0.0678$	$F_{(1, 67)} = 6.9$ $P = 0.0107$	CTL-Sal vs CTL-PRZP $P = 0.0093$ / **
	CTL-PRZP	18	1.363 $\pm$ 0.0218					KI-Sal vs KI-PRZP $P = 0.9301$ / N.S.
	KI-Sal	16	1.509 $\pm$ 0.0340					
	KI-PRZP	18	1.54 $\pm$ 0.0442					
100	CTL-Sal	18	1.435 $\pm$ 0.0340	Two-way ANOVA	$F_{(1, 67)} = 3.845$ $p = 0.0540$	$F_{(1, 67)} = 0.0972$ $p = 0.7562$	$F_{(1, 67)} = 3.302$ $p = 0.0737$	CTL-Sal vs CTL-PRZP $P = 0.0961$ / N.S.
	CTL-PRZP	18	1.359 $\pm$ 0.0281					KI-Sal vs KI-PRZP $P = 0.2578$ / N.S.
	KI-Sal	16	1.428 $\pm$ 0.0407					
	KI-PRZP	18	1.485 $\pm$ 0.0322					
200	CTL-Sal	18	1.196 $\pm$ 0.0260	Two-way ANOVA	$F_{(1, 67)} = 1.415$ $P = 0.2384$	$F_{(1, 67)} = 0.0516$ $P = 0.8210$	$F_{(1, 67)} = 2.184$ $P = 0.1441$	CTL-Sal vs CTL-PRZP $P = 0.9022$ / N.S.
	CTL-PRZP	18	1.226 $\pm$ 0.0232					KI-Sal vs KI-PRZP $P = 0.7529$ / N.S.
	KI-Sal	16	1.268 $\pm$ 0.0452					
	KI-PRZP	18	1.235 $\pm$ 0.0290					
400	CTL-Sal	18	1.077 $\pm$ 0.0269	Two-way ANOVA	$F_{(1, 67)} = 0.6877$ $P = 0.4099$	$F_{(1, 67)} = 1.272$ $P = 0.2635$	$F_{(1, 67)} = 0.0433$ $P = 0.8358$	CTL-Sal vs CTL-PRZP $P = 0.9966$ / N.S.
	CTL-PRZP	18	1.07 $\pm$ 0.0143					KI-Sal vs KI-PRZP $P = 0.5200$ / N.S.
	KI-Sal	16	1.079 $\pm$ 0.0188					
	KI-PRZP	18	1.055 $\pm$ 0.0233					
500	CTL-Sal	18	1.045 $\pm$ 0.0211	Two-way ANOVA	$F_{(1, 67)} = 0.1621$ $P = 0.6885$	$F_{(1, 67)} = 0.0194$ $P = 0.8896$	$F_{(1, 67)} = 5.915$ $P = 0.0177$	CTL-Sal vs CTL-PRZP $P = 0.9976$ / N.S.
	CTL-PRZP	18	1.051 $\pm$ 0.0157					KI-Sal vs KI-PRZP $P = 0.9811$ / N.S.
	KI-Sal	16	1.092 $\pm$ 0.0228					
	KI-PRZP	18	1.101 $\pm$ 0.0277					

**Fig. 7a**

Group	N number	Mean ±S.E.M	One-way ANOVA	P-value /Significance	
No Cort	8	121.3 ± 7.690	$F_{(2, 23)} = 6.616$ $P = 0.0054$	No Cort vs Cort-Sal	$P = 0.0050$ / **
Cort-Sal	9	152.0 ± 5.475		No Cort vs Cort-Ket	$P = 0.5290$ / N.S.
Cort-Ket	9	130.8 ± 5.214		Cort-Sal vs Cort-Ket	$P = 0.499$ / *

**Fig. 7b**

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Time factor	Drug factor	P-value /Significance			
24 h	Sal	9	149.3 ± 6.972	Two-way RM ANOVA	$F_{(1, 17)} = 0.0670$ $P = 0.7989$	$F_{(1, 17)} = 2.386$ $P = 0.1408$	$F_{(1, 17)} = 19.18$ $P = 0.0004$	24h: Sal vs SCA $P = 0.0065$ / **			
	SCA	10	126.2 ± 3.402					24h: Sal vs SCA $P = 0.0026$ / **			
7 days	Sal	9	157.9 ± 5.298								
	SCA	10	132.3 ± 4.768								

**Extended Data Fig. 1**

Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
Sal	8	1.0 ± 0.1457	Unpaired t-test	$t_{(14)} = 0.3298$ $P = 0.7464$ / N.S.
Ket	8	1.068 ± 0.1463		

**Extended Data Fig. 2**

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance			
CTL	Sal	7	1.0 ± 0.1596	Two-way ANOVA	$F_{(1, 21)} = 0.0157$ $P = 0.9016$	$F_{(1, 21)} = 0.0115$ $P = 0.9158$	$F_{(1, 21)} = 31.93$ $P < 0.0001$	CTL-Sal vs CTL-Ket $P = 0.0014$ / **			
	Ket	7	1.964 ± 0.1162					KI-Sal vs KI-Ket $P = 0.0069$ / **			
<i>Mecp2</i> KI	Sal	6	1.039 ± 0.1823								
	Ket	5	1.961 ± 0.2186								

**Extended Data Fig. 3a**

Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
Sal-Base	9	4.128 ± 0.5270	Unpaired t-test	$t_{(17)} = 1.448, P = 0.1659$ / N.S.
Ket-Base	10	5.494 ± 0.7581		

Extended Data Fig. 3b

Interstimulus interval	Group		N number	Mean $\pm$ S.E.M	Statistics	Interaction	Pretreatment factor	Ketamine factor
20	Sal-Ket	before	11	1.385 $\pm$ 0.0336	Two-way ANOVA	$F_{(1, 38)} = 0.1944$ $P = 0.6618$	$F_{(1, 38)} = 0.4597$ $P = 0.5019$	$F_{(1, 38)} = 1.174$ $P = 0.2854$
		after	11	1.359 $\pm$ 0.0445				
	Ket-Ket	before	10	1.376 $\pm$ 0.0460				
		after	10	1.315 $\pm$ 0.0316				
30	Sal-Ket	before	11	1.476 $\pm$ 0.0318	Two-way ANOVA	$F_{(1, 38)} = 0.0682$ $P = 0.7954$	$F_{(1, 38)} = 1.111$ $P = 0.2985$	$F_{(1, 38)} = 0.6195$ $P = 0.4361$
		after	11	1.455 $\pm$ 0.0471				
	Ket-Ket	before	10	1.444 $\pm$ 0.0473				
		after	10	1.402 $\pm$ 0.0335				
50	Sal-Ket	before	11	1.555 $\pm$ 0.0291	Two-way ANOVA	$F_{(1, 38)} = 0.1586$ $P = 0.6927$	$F(1, 38) = 0.8878$ $P = 0.3520$	$F_{(1, 38)} = 0.0068$ $P = 0.9345$
		after	11	1.542 $\pm$ 0.0442				
	Ket-Ket	before	10	1.499 $\pm$ 0.0361				
		after	10	1.519 $\pm$ 0.0547				
100	Sal-Ket	before	11	1.457 $\pm$ 0.0359	Two-way ANOVA	$F_{(1, 38)} = 0.0307$ $P = 0.8619$	$F_{(1, 38)} = 0.0732$ $P = 0.7882$	$F_{(1, 38)} = 0.2228$ $P = 0.6396$
		after	11	1.480 $\pm$ 0.0442				
	Ket-Ket	before	10	1.454 $\pm$ 0.0244				
		after	10	1.464 $\pm$ 0.0323				
200	Sal-Ket	before	11	1.259 $\pm$ 0.0273	Two-way ANOVA	$F_{(1, 38)} = 0.7025$ $P = 0.4072$	$F_{(1, 38)} = 0.8733$ $P = 0.3560$	$F_{(1, 38)} = 0.4935$ $P = 0.4866$
		after	11	1.311 $\pm$ 0.0265				
	Ket-Ket	before	10	1.256 $\pm$ 0.1524				
		after	10	1.252 $\pm$ 0.0300				
400	Sal-Ket	before	11	1.091 $\pm$ 0.0177	Two-way ANOVA	$F_{(1, 38)} = 0.1475$ $P = 0.7030$	$F_{(1, 38)} = 0.0614$ $P = 0.8056$	$F_{(1, 38)} = 0.4658$ $P = 0.4991$
		after	11	1.097 $\pm$ 0.0552				
	Ket-Ket	before	10	1.078 $\pm$ 0.0247				
		after	10	1.100 $\pm$ 0.0238				
500	Sal-Ket	before	11	1.078 $\pm$ 0.0159	Two-way ANOVA	$F_{(1, 38)} = 0.8473$ $P = 0.3631$	$F_{(1, 38)} = 2.472$ $P = 0.1242$	$F_{(1, 38)} = 1.349$ $P = 0.2528$
		after	11	1.081 $\pm$ 0.0131				
	Ket-Ket	before	10	1.046 $\pm$ 0.0082				
		after	10	1.072 $\pm$ 0.0119				



**Extended Data Fig. 4a,b**

Pre-treatment	Perfusion	N number	Mean ±S.E.M	Statistics	P-value /Significance
Sal(i.p.)	ACSF	6	97.46 ± 2.112	Unpaired t-test	Sal-ACSF vs Sal-Ket $t_{(11)} = 4.207, P = 0.0015 / **$
	Ket	7	114 ± 3.158		Ket-ACSF vs Ket-Ket $t_{(10)} = 5.528, P = 0.0003 / ***$
Ket (i.p.)	ACSF	6	97.7 ± 3.064		Sal-Ket vs Ket-Ket $t_{(11)} = 3.465, P = 0.0053 / **$
	Ket	6	138.5 ± 6.717		

**Extended Data Fig. 5a,b**

	Time	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
pCaMKII $\alpha$ /CaMKII $\alpha$	3 days	Sal	8	1.0 ± 0.0854	Unpaired t-test	$t_{(14)} = 0.4369$ $P = 0.6688 / N.S.$
		Ket	8	1.064 ± 0.1178		
	7 days	Sal	8	1.0 ± 0.1146	Unpaired t-test	$t_{(14)} = 1.052$ $P = 0.3107 / N.S.$
		Ket	8	1.219 ± 0.1734		
pCaMKII $\beta$ /CaMKII $\beta$	3 days	Sal	8	1.0 ± 0.1134	Unpaired t-test	$t_{(14)} = 3.756$ $P = 0.0021 / **$
		Ket	8	1.638 ± 0.1264		
	7 days	Sal	8	1.0 ± 0.1915	Unpaired t-test	$t_{(14)} = 0.3796$ $P = 0.7100 / N.S.$
		Ket	8	1.116 ± 0.2385		
pMeCP2/MeCP2	3 days	Sal	9	1.0 ± 0.1889	Unpaired t-test	$t_{(16)} = 2.332$ $P = 0.0331 / *$
		Ket	9	1.610 ± 0.1811		
	7 days	Sal	8	1.0 ± 0.1894	Unpaired t-test	$t_{(14)} = 2.440$ $P = 0.0286 / *$
		Ket	8	2.053 ± 0.3879		
BDNF/GAPDH	3 days	Sal	8	1.0 ± 0.0826	Unpaired t-test	$t_{(14)} = 0.0433$ $P = 0.9661 / N.S.$
		Ket	8	1.007 ± 0.1401		

**Extended Data Fig. 6a**

Time	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
7 days	Sal	10	131.4 ± 7.538	Unpaired t-test	$t_{(17)} = 2.469, P = 0.0244 / *$
	SCA	9	92.78 ± 14.23		

**Extended Data Fig. 6b**

Interstimulus interval	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
20	Sal	24	1.4 ± 0.0430	Mann-Whitney test	$U = 210, P = 0.0314 / *$
	SCA	27	1.276 ± 0.0287		
30	Sal	24	1.474 ± 0.0377	Mann-Whitney test	$U = 207, P = 0.0270 / *$
	SCA	27	1.359 ± 0.0366		
50	Sal	24	1.476 ± 0.0358	Unpaired t-test	$t_{(49)} = 0.6624, P = 0.5108 / \text{N.S.}$
	SCA	27	1.442 ± 0.0366		
100	Sal	24	1.448 ± 0.0312	Mann-Whitney test	$U = 265, P = 0.2722 / \text{N.S.}$
	SCA	27	1.403 ± 0.0293		
200	Sal	24	1.258 ± 0.0277	Unpaired t-test	$t_{(49)} = 1.137, P = 0.2612 / \text{N.S.}$
	SCA	27	1.218 ± 0.0225		
400	Sal	24	1.103 ± 0.0247	Unpaired t-test	$t_{(49)} = 0.7955, P = 0.4302 / \text{N.S.}$
	SCA	27	1.080 ± 0.0156		
500	Sal	24	1.074 ± 0.0195	Unpaired t-test	$t_{(49)} = 49, P = 0.3527 / \text{N.S.}$
	SCA	27	1.052 ± 0.0134		

**Extended Data Fig. 7**

Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
ActD-Sal	10	140 ± 5.534	Unpaired t-test	$t_{(17)} = 1.006$ $P = 0.3286 / \text{N.S.}$
ActD-SCA	9	132.2 ± 5.348		

**Extended Data Fig. 8**

Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
Sal	8	1.0 ± 0.1685	Unpaired t-test	$t_{(14)} = 0.0705$ $P = 0.9448 / \text{N.S.}$
SCA	8	0.9833 ± 0.1658		

**Extended Data Fig. 9**

Time	Group	N number	Mean ±S.E.M	Statistics	P-value /Significance
8 h	Sal	8	1.0 ± 0.1218	Welch's correction	$t_{(9,272)} = 0.9004, P = 0.3907 / \text{N.S.}$
	SCA	8	1.290 ± 0.2983		
24 h	Sal	7	1.0 ± 0.1756	Unpaired t-test	$t_{(12)} = 0.0677, P = 0.9472 / \text{N.S.}$
	SCA	7	0.9831 ± 0.1781		

**Extended Data Fig. 10**

Genotype	Group	N number	Mean ±S.E.M	Statistics	Interaction	Genotype factor	Drug factor	P-value /Significance			
CTL	Sal	10	1.0 ± 0.0623	Two-way ANOVA	$F_{(1,33)} = 0.0467$ $P = 0.8302$	$F_{(1,33)} = 0.3223$ $P = 0.5741$	$F_{(1,33)} = 19.22$ $P = 0.0001$	CTL-Sal vs CTL- SCA $P = 0.0207 / *$			
	SCA	9	1.318 ± 0.0913					KI-Sal vs KI-SCA $P = 0.0184 / *$			
<i>Mecp2</i> KI	Sal	10	0.9402 ± 0.0399								
	SCA	8	1.291 ± 0.0987								