

## Supplemental material

**Table S1.** Electrophysiological intervals and cardiac refractory periods from wild-type (WT) vehicle, wild-type propranolol, *Mecp2*<sup>Null/Y</sup> vehicle, and *Mecp2*<sup>Null/Y</sup> propranolol treated mice at 2 months old. Data are expressed as means ± SEM. RR, interval between two consecutive R waves; PQ, interval from the start of the P wave to the peak of the Q wave; QRS, interval from the start of the Q wave to the peak of the S wave; QT, duration from the beginning of the Q wave to the end of the T wave; QTc, corrected QT interval for heart rate; SNRT, sinoatrial node refractory time defined as the last atrial pace to the first A wave; AVERP, time between pacing stimulus when atrioventricular node does not conduct; VERP, time between pacing cycle that causes ventricular refractory period. Statistical analysis was conducted for genotype and treatment effects followed by a one way ANOVA for multiple comparisons.

	Vehicle		Propranolol	
	<i>Mecp2</i> <sup>+Y</sup> (2 months) (n=8)	<i>Mecp2</i> <sup>Null/Y</sup> (2 months) (n=8)	<i>Mecp2</i> <sup>+Y</sup> (2 months) (n=8)	<i>Mecp2</i> <sup>Null/Y</sup> (2 months) (n=8)
<b>RR (ms)</b>	123.0 ± 5.9	115.2 ± 4.0	127.7 ± 6.3	119.5 ± 2.0
<b>PQ (ms)</b>	35.3 ± 0.4	34.6 ± 0.6	35.9 ± 0.9	35.2 ± 0.7
<b>QRS (ms)</b>	8.5 ± 0.1	9.4 ± 0.3 <sup>†*</sup>	8.5 ± 0.2	10.3 ± 0.2 <sup>†***</sup>
<b>QT (ms)</b>	33.2 ± 1.4	43.1 ± 1.3 <sup>†**</sup>	35.2 ± 2.0	42.5 ± 1.0 <sup>†*</sup>
<b>QTc (ms)</b>	48.1 ± 1.3	60.5 ± 0.8 <sup>†***</sup>	48.6 ± 1.8	58.5 ± 1.0 <sup>†***</sup>
<b>SNRT (ms)</b>	142.9 ± 9.7	132.0 ± 7.2	167.8 ± 11 <sup>δ</sup>	162.0 ± 12 <sup>δ</sup>
<b>AVERP (ms)</b>	44.8 ± 1.5	42.4 ± 1.4	46.0 ± 2.2	45.2 ± 1.9
<b>VERP (ms)</b>	23.3 ± 1.2	23.6 ± 1.7	23.8 ± 1.6	23.1 ± 1.0

Genotype effect: WT vs *Mecp2*<sup>Null/Y</sup> † p<0.001; Treatment effect: vehicle vs propranolol <sup>δ</sup> p<0.05; ANOVA Tukey's post hoc *Mecp2*<sup>Null/Y</sup> vehicle or propranolol vs WT vehicle or propranolol \* p<0.05, \*\* p<0.01, \*\*\* p<0.001

**Table S2.** Electrophysiological intervals and cardiac refractory periods from wild-type (WT) vehicle, wild-type propranolol, *Mecp2*<sup>Null/+</sup> vehicle, and *Mecp2*<sup>Null/+</sup> propranolol treated mice at 10 months old. Data are expressed as means ± SEM.

	Vehicle		Propranolol	
	<i>Mecp2</i> <sup>+/+</sup> (10 months) (n=9)	<i>Mecp2</i> <sup>Null/+</sup> (10 months) (n=9)	<i>Mecp2</i> <sup>+/+</sup> (10 months) (n=8)	<i>Mecp2</i> <sup>Null/+</sup> (10 months) (n=9)
<b>RR (ms)</b>	124.4 ± 2.7	128.4 ± 3.0	138.4 ± 4.7 <sup>δ</sup>	129.4 ± 2.9 <sup>δ</sup>
<b>PQ (ms)</b>	35.7 ± 0.6	36.9 ± 0.7	36.9 ± 0.8	37.8 ± 1.2
<b>QRS (ms)</b>	8.1 ± 0.1	9.9 ± 0.2 <sup>†***</sup>	8.4 ± 0.2	10.0 ± 0.1 <sup>†***</sup>
<b>QT (ms)</b>	33.4 ± 1.1	39.1 ± 1.2 <sup>ς</sup>	38.4 ± 1.9 <sup>δ*</sup>	40.3 ± 1.1 <sup>δ*</sup>
<b>QTc (ms)</b>	47.9 ± 0.6	52.3 ± 0.7 <sup>†**</sup>	48.4 ± 0.8	53.2 ± 0.8 <sup>†**</sup>
<b>SNRT</b>	145.1 ± 7.7	129.0 ± 4.3	182.1 ± 12 <sup>δ</sup>	155.1 ± 9.0 <sup>δ</sup>
<b>AVERP</b>	44.6 ± 0.8	44.4 ± 1.0	47.4 ± 1.6	47.0 ± 2.0
<b>VERP</b>	22.8 ± 1.1	22.4 ± 1.1	23.8 ± 1.2	24.2 ± 1.8

Genotype effect: WT vs *Mecp2*<sup>Null/Y</sup> † p<0.001, ς p<0.01 ^ p<0.05; Treatment effect: vehicle vs propranolol δ p<0.05 ANOVA Tukey's post hoc *Mecp2*<sup>Null/Y</sup> vehicle or propranolol vs WT vehicle or propranolol \* p<0.05, \*\* p<0.01, \*\*\* p<0.001

**Table S3.** Electrophysiological intervals and cardiac refractory periods from wild-type (WT) vehicle, wild-type phenytoin, *Mecp2*<sup>Null/Y</sup> vehicle, and *Mecp2*<sup>Null/Y</sup> phenytoin treated mice at 2 months old. Data are expressed as means ± SEM.

	Vehicle		Phenytoin	
	<i>Mecp2</i> <sup>+Y</sup> (2 months) (n=9)	<i>Mecp2</i> <sup>Null/Y</sup> (2 months) (n=7)	<i>Mecp2</i> <sup>+Y</sup> (2 months) (n=8)	<i>Mecp2</i> <sup>Null/Y</sup> (2 months) (n=8)
<b>RR (ms)</b>	119.3 ± 2.9	113.9 ± 4.2	115.4 ± 3.8	122.2 ± 5.3
<b>PQ (ms)</b>	35.0 ± 0.3	35.4 ± 0.3	33.3 ± 0.6	33.5 ± 0.8
<b>QRS (ms)</b>	8.3 ± 0.2	9.9 ± 0.2 <sup>***</sup>	8.5 ± 0.1	7.9 ± 0.2
<b>QT (ms)</b>	31.4 ± 1.3	42.0 ± 0.9 <sup>**</sup>	32.2 ± 1.4	36.0 ± 2.5
<b>QTc (ms)</b>	47.5 ± 0.8	60.0 ± 0.8 <sup>***</sup>	49.6 ± 1.1	51.2 ± 1.3
<b>SNRT</b>	134.6 ± 4.8	140.1 ± 11	156.8 ± 11	140.0 ± 9.5
<b>AVERP</b>	45.5 ± 1.1	43.5 ± 3.7	44.5 ± 1.6	47.6 ± 2.3
<b>VERP</b>	23.7 ± 1.2	24.7 ± 1.4	24.0 ± 1.1	23.8 ± 1.8

ANOVA Tukey's post hoc QRS and QTc *Mecp2*<sup>Null/Y</sup> vehicle vs *Mecp2*<sup>Null/Y</sup> phenytoin, WT vehicle, or WT phenytoin<sup>\*\*\*</sup> p<0.001; QT *Mecp2*<sup>Null/Y</sup> vehicle vs WT vehicle or WT phenytoin<sup>\*\*\*</sup> p<0.001

**Table S4.** Electrophysiological intervals and cardiac refractory periods from wild-type (WT) vehicle, wild-type phenytoin, *Mecp2*<sup>Null/+</sup> vehicle, and *Mecp2*<sup>Null/+</sup> phenytoin treated mice at 10 months old. Data are expressed as means ± SEM.

	Vehicle		Phenytoin	
	<i>Mecp2</i> <sup>+/+</sup> (10 months) (n=10)	<i>Mecp2</i> <sup>Null/+</sup> (10 months) (n=9)	<i>Mecp2</i> <sup>+/+</sup> (10 months) (n=9)	<i>Mecp2</i> <sup>Null/+</sup> (10 months) (n=9)
<b>RR (ms)</b>	119.0 ± 3.3	115.3 ± 2.5	115.4 ± 2.6	123.6 ± 3.6
<b>PQ (ms)</b>	35.9 ± 0.5	34.0 ± 0.6	35.2 ± 0.7	36.9 ± 0.7*
<b>QRS (ms)</b>	7.9 ± 0.1	9.9 ± 0.1***	8.0 ± 0.1	8.1 ± 0.1
<b>QT (ms)</b>	32.8 ± 1.2	37.6 ± 0.7**	31.6 ± 0.8	35.1 ± 1.2
<b>QTc (ms)</b>	49.0 ± 0.2	55.0 ± 0.8***	48.9 ± 0.4	49.8 ± 0.4
<b>SNRT</b>	138.8 ± 5.8	153.1 ± 8.7**	128.9 ± 4.1	166.1 ± 7.8
<b>AVERP</b>	45.1 ± 0.8	45.4 ± 1.5*	42.0 ± 1.7	50.6 ± 1.4
<b>VERP</b>	22.3 ± 1.1	24.4 ± 1.5	25.0 ± 1.1	27.2 ± 0.8

ANOVA Tukey's post hoc PQ: *Mecp2*<sup>Null/+</sup> vehicle vs *Mecp2*<sup>Null/+</sup> phenytoin \* p<0.05; QRS and QTc: *Mecp2*<sup>Null/+</sup> vehicle vs *Mecp2*<sup>Null/+</sup> phenytoin, WT vehicle, or WT phenytoin\*\*\* p<0.001; QT: *Mecp2*<sup>Null/+</sup> vehicle vs WT vehicle or WT phenytoin\*\* p<0.01; SNRT: *Mecp2*<sup>Null/+</sup> vehicle vs *Mecp2*<sup>Null/+</sup> phenytoin \*\*p<0.01; AVERP: *Mecp2*<sup>Null/+</sup> vehicle vs *Mecp2*<sup>Null/+</sup> phenytoin \*p<0.05