

**Table S1. Properties of SCN PER2::LUC rhythms ( $\pm$  SEM) prior to manipulation (averaged across slice position).**

Experiment	Manipulation	Genotype	Sex	n	Phase (CT)	Period (h)	Damping (days)	Prediction Error (h)
1a <sup>§</sup>	V1A/B Dose, +V1A/B Antag	PER2::LUC	<b>Both</b>	<b>56</b>	<b>10.8 <math>\pm</math> 0.1</b>	<b>24.47 <math>\pm</math> 0.04*</b>	<b>3.8 <math>\pm</math> 0.2</b>	<b>0.03 <math>\pm</math> 0.03</b>
			Female	26	10.9 $\pm$ 0.1	24.58 $\pm$ 0.06	3.6 $\pm$ 0.4	0.07 $\pm$ 0.06
			Male	30	10.8 $\pm$ 0.1	24.37 $\pm$ 0.05	3.9 $\pm$ 0.2	-0.003 $\pm$ 0.02
1b <sup>§</sup>	V1A, V1B	PER2::LUC	<b>Both</b>	<b>46</b>	<b>11.3 <math>\pm</math> 0.2</b>	<b>24.51 <math>\pm</math> 0.04*</b>	<b>3.9 <math>\pm</math> 0.3</b>	<b>-0.02 <math>\pm</math> 0.04</b>
			Female	22	11.6 $\pm$ 0.3	24.65 $\pm$ 0.05	3.6 $\pm$ 0.3	0.06 $\pm$ 0.07
			Male	24	11.1 $\pm$ 0.3	24.38 $\pm$ 0.06	4.1 $\pm$ 0.5	-0.02 $\pm$ 0.03
2 <sup>§</sup>	PRC	PER2::LUC	<b>Both</b>	<b>53</b>	<b>10.8 <math>\pm</math> 0.1*</b>	<b>24.54 <math>\pm</math> 0.03</b>	<b>3.4 <math>\pm</math> 0.1</b>	<b>0.01 <math>\pm</math> 0.02</b>
			Female	24	11.0 $\pm$ 0.2	24.54 $\pm$ 0.05	3.2 $\pm$ 0.1	-0.03 $\pm$ 0.02
			Male	29	10.7 $\pm$ 0.1	24.53 $\pm$ 0.04	3.5 $\pm$ 0.2	0.04 $\pm$ 0.03
3 <sup>§</sup>	PLC, AC Inhibitors	PER2::LUC	<b>Both</b>	<b>37</b>	<b>11.2 <math>\pm</math> 0.1</b>	<b>24.51 <math>\pm</math> 0.03*</b>	<b>4.0 <math>\pm</math> 0.2*</b>	<b>-0.02 <math>\pm</math> 0.02</b>
			Female	21	11.0 $\pm$ 0.1	24.63 $\pm$ 0.04	3.5 $\pm$ 0.9	-0.06 $\pm$ 0.02
			Male	16	10.9 $\pm$ 0.2	24.48 $\pm$ 0.03	4.1 $\pm$ 0.2	-0.02 $\pm$ 0.03
4a <sup>§</sup>	VIP WT	<i>Vip</i> <sup>+/+</sup> ; PER2::LUC	<b>Both</b>	<b>28</b>	<b>10.8 <math>\pm</math> 0.2</b>	<b>24.45 <math>\pm</math> 0.06*</b>	<b>3.2 <math>\pm</math> 0.1</b>	<b>0.04 <math>\pm</math> 0.06</b>
			Female	12	11.1 $\pm$ 0.2	24.62 $\pm$ 0.07	3.0 $\pm$ 0.1	0.14 $\pm$ 0.13
			Male	16	10.7 $\pm$ 0.2	24.32 $\pm$ 0.07	3.3 $\pm$ 0.1	-0.03 $\pm$ 0.04
	VIP Deficient Heterozygous	<i>Vip</i> <sup>cre/+</sup> ; PER2::LUC	<b>Both</b>	<b>17</b>	<b>10.5 <math>\pm</math> 0.1</b>	<b>24.34 <math>\pm</math> 0.05*</b>	<b>3.7 <math>\pm</math> 0.1*</b>	<b>0.04 <math>\pm</math> 0.05</b>
			Female	10	10.4 $\pm$ 0.2 <sup>‡</sup>	24.21 $\pm$ 0.05 <sup>‡</sup>	3.5 $\pm$ 0.1 <sup>‡</sup>	0.005 $\pm$ 0.05
			Male	7	10.7 $\pm$ 0.3	24.51 $\pm$ 0.07	3.9 $\pm$ 0.1 <sup>‡</sup>	-0.10 $\pm$ 0.1
	VIP Deficient Homozygous	<i>Vip</i> <sup>cre/cre</sup> ; PER2::LUC	<b>Both</b>	<b>16</b>	<b>10.1 <math>\pm</math> 0.1</b>	<b>24.45 <math>\pm</math> 0.05</b>	<b>4.4 <math>\pm</math> 0.1</b>	<b>0.01 <math>\pm</math> 0.03</b>
			Female	10	10.0 $\pm$ 0.1 <sup>‡</sup>	24.39 $\pm$ 0.05 <sup>‡</sup>	4.4 $\pm$ 0.1 <sup>‡</sup>	0.02 $\pm$ 0.04
			Male	6	10.1 $\pm$ 0.3	24.55 $\pm$ 0.08 <sup>‡</sup>	4.5 $\pm$ 0.3 <sup>‡</sup>	-0.01 $\pm$ 0.04
4b <sup>§</sup>	VPAC2 Antagonist	PER2::LUC	<b>Both</b>	<b>12</b>	<b>11.2 <math>\pm</math> 0.2</b>	<b>24.53 <math>\pm</math> 0.05</b>	<b>3.5 <math>\pm</math> 0.1</b>	<b>-0.04 <math>\pm</math> 0.03</b>
			Female	6	11.4 $\pm$ 0.2	24.54 $\pm$ 0.07	3.3 $\pm$ 0.1	0.01 $\pm$ 0.04
			Male	6	10.9 $\pm$ 0.2	24.51 $\pm$ 0.08	3.6 $\pm$ 0.2	-0.08 $\pm$ 0.03
Overall <sup>§</sup>	Multiple	PER2::LUC WT	<b>Both</b>	<b>204</b>	<b>11.1 <math>\pm</math> 0.1*</b>	<b>24.52 <math>\pm</math> 0.02*</b>	<b>3.8 <math>\pm</math> 0.1</b>	<b>-0.01 <math>\pm</math> 0.01</b>
			Female	99	11.2 $\pm$ 0.1	24.57 $\pm$ 0.02	3.6 $\pm$ 0.1	-0.06 $\pm$ 0.03
			Male	105	10.9 $\pm$ 0.1	24.48 $\pm$ 0.03	3.9 $\pm$ 0.2	-0.10 $\pm$ 0.02

<sup>§</sup>1a- **Phase:**  $t(54) = -0.4, p > 0.6$ , **Period:**  $t(54) = -2.5, p = 0.02$ , **Damping:**  $t(54) = 0.6, p > 0.5$ , **Prediction Error:**  $t(54) = -1.1, p > 0.2$

<sup>§</sup>1b- **Phase:**  $t(44) = -1.15, p > 0.2$ , **Period:**  $t(44) = -3.6, p < 0.001$ , **Damping:**  $t(44) = 0.7, p > 0.4$ , **Prediction Error:**  $t(44) = -1.1, p > 0.2$

<sup>§</sup>2- **Phase:**  $t(51) = -1.7, p = 0.09$ , **Period:**  $t(51) = -0.07, p > 0.9$ , **Damping:**  $t(51) = 1.0, p > 0.3$ , **Prediction Error:**  $t(51) = -1.9, p = 0.06$

<sup>§</sup>3- **Phase:**  $t(35) = -0.4, p > 0.7$ , **Period:**  $t(35) = -2.6, p = 0.01$ , **Damping:**  $t(35) = 3.3, p < 0.05$ , **Prediction Error:**  $t(35) = 1.1, p > 0.2$

<sup>§</sup>4a- **Phase:** Genotype:  $F(2,55) = 6.5, p = 0.003$ , Sex:  $F(1,55) = 0.01, p > 0.9$ , Genotype\*Sex:  $F(2,55) = 1.5, p > 0.2$ , **Period:** Genotype:  $F(2,55) = 1.6, p > 0.2$ , Sex:  $F(1,55) = 0.9, p > 0.3$ , Genotype\*Sex:  $F(2,55) = 11.7, p < 0.0001$ , **Damping:** Genotype:  $F(2,55) = 1.7, p > 0.1$ , Sex:  $F(1,55) = 0.01, p > 0.9$ , Genotype\*Sex:  $F(2,55) = 0.09, p > 0.9$ , **Prediction Error:** Genotype:  $F(2,55) = 0.2, p > 0.7$ , Sex:  $F(1,55) = 0.3, p > 0.6$ , Genotype\*Sex:  $F(2,55) = 1.5, p > 0.2$

<sup>§</sup>4b- **Phase:**  $t(10) = -1.7, p = 0.09$ , **Period:**  $t(10) = -0.2, p > 0.8$ , **Damping:**  $t(10) = 1.43, p > 0.1$ , **Prediction Error:**  $t(10) = -1.7, p > 0.1$

<sup>§</sup>Overall- **Phase:**  $t(210) = -2.2, p = 0.03$ , **Period:**  $t(210) = -2.4, p = 0.02$ , **Damping:**  $t(210) = 1.8, p = 0.7$ , **Prediction Error:**  $t(210) = -1.3, p > 0.2$

\* Sex difference,  $p < 0.05$ . <sup>‡</sup> Genotype difference,  $p < 0.05$

Table S2. Properties of SCN PER2::LUC rhythms ( $\pm$ SEM) after treatment (averaged across slice position).

Experiment	Manipulation	V1 Group	n	Phase Shift (h)			Period Difference (h)			Damping (days)		
				Both	Female	Male	Both	Female	Male	Both	Female	Male
1a <sup>§</sup>	0uM	Vehicle	10	0.3 ± 0.2	0.5 ± 0.2	0.0 ± 0.2	0.02 ± 0.2	0.21 ± 0.2	-0.16 ± 0.3	4.2 ± 0.5	3.8 ± 0.9	4.6 ± 0.3
	1uM	Agonists	7	-0.4 ± 0.2 <sup>#</sup>	-0.2 ± 0.3 <sup>#</sup>	-0.7 ± 0.2	-0.31 ± 0.3	-0.57 ± 0.5 <sup>#</sup>	0.03 ± 0.3	4.3 ± 0.5	4.9 ± 0.7	3.5 ± 0.6
	5uM	Agonists	7	-0.1 ± 0.1	-0.2 ± 0.2 <sup>#</sup>	-0.1 ± 0.1	-0.48 ± 0.3 <sup>#</sup>	-0.32 ± 0.4	-0.70 ± 0.3	3.7 ± 0.5	3.8 ± 0.9	3.6 ± 0.5
	10uM	Agonists	18	-0.9 ± 0.1 <sup>#*</sup>	-1.3 ± 0.3 <sup>#</sup>	-0.6 ± 0.1 <sup>#</sup>	0.08 ± 0.1	-0.05 ± 0.1	0.16 ± 0.1	3.5 ± 0.4	2.9 ± 0.2	3.9 ± 0.6
	50uM	Agonists	5	0.0 ± 0.3	0.2 ± 0.3	-0.1 ± 0.5	-0.53 ± 0.1 <sup>#</sup>	-0.80 ± 0.2 <sup>#</sup>	-0.35 ± 0.1	5.0 ± 1.0	5.4 ± 2.5	4.8 ± 1.1
1b <sup>§</sup>	V1 Antagonists	Agonists	9	0.2 ± 0.3	0.0 ± 0.5	0.3 ± 0.3	0.33 ± 0.2 <sup>*</sup>	0.74 ± 0.4	0.01 ± 0.2	3.6 ± 0.4	3.2 ± 0.5	4.0 ± 0.7
	Vehicle	Vehicle	23	-0.1 ± 0.1	0.3 ± 0.1	-0.2 ± 0.2	-0.08 ± 0.1	-0.11 ± 0.1	-0.04 ± 0.1	4.9 ± 0.7	4.1 ± 0.6	6.1 ± 1.3
	V1A/B	Agonists	35	-0.7 ± 0.1 <sup>#</sup>	-0.8 ± 0.2 <sup>#</sup>	-0.5 ± 0.1	0.12 ± 0.1	0.06 ± 0.1	0.18 ± 0.1	3.8 ± 0.4	3.1 ± 0.2	4.3 ± 0.7
	V1A	Agonist	9	-0.4 ± 0.2 <sup>#</sup>	-0.5 ± 0.1 <sup>#</sup>	-0.4 ± 0.5	-0.27 ± 0.2	-0.29 ± 0.1	-0.17 ± 0.1	3.3 ± 0.5	3.2 ± 0.4	3.5 ± 0.9
	V1B	Agonist	8	-0.2 ± 0.2	-0.2 ± 0.3	-0.3 ± 0.1	-0.34 ± 0.2	-0.08 ± 0.2	-0.30 ± 0.1	3.6 ± 0.3	3.1 ± 0.3	4.5 ± 0.2
2 <sup>§</sup>	CT04	Vehicle	6	0.6 ± 0.2	0.8 ± 0.2	0.3 ± 0.4	0.20 ± 0.2	0.35 ± 0.1	0.06 ± 0.3	4.8 ± 0.6	4.5 ± 1.1	5.0 ± 0.5
	CT10	Agonists	11	0.0 ± 0.1 <sup>#</sup>	0.1 ± 0.1	-0.1 ± 0.2	0.10 ± 0.1	0.04 ± 0.2	0.16 ± 0.1	4.0 ± 0.7	3.1 ± 0.2	4.8 ± 1.3
		Vehicle	8	-0.4 ± 0.2	-0.4 ± 0.2	-0.4 ± 0.3	0.10 ± 0.1	-0.12 ± 0.2	0.32 ± 0.1	3.2 ± 0.3	3.6 ± 0.5	2.9 ± 0.2
	CT16	Agonists	10	0.0 ± 0.2	0.2 ± 0.1	-0.1 ± 0.4	0.01 ± 0.1	0.16 ± 0.1	0.01 ± 0.1	4.1 ± 0.5	3.5 ± 0.5	4.5 ± 0.7
		Vehicle	9	-0.5 ± 0.2	-0.4 ± 0.3	-0.7 ± 0.3	-0.38 ± 0.1 <sup>*</sup>	-0.45 ± 0.2	-0.32 ± 0.1	2.8 ± 0.5	3.3 ± 0.6	3.2 ± 0.4
	CT22	Agonists	9	-1.1 ± 0.1 <sup>#</sup>	-1.0 ± 0.3	-1.2 ± 0.1	-0.38 ± 0.1 <sup>*</sup>	-0.74 ± 0.2	-0.09 ± 0.1	5.2 ± 0.7 <sup>#</sup>	4.6 ± 0.4	5.7 ± 1.3 <sup>#</sup>
		Vehicle	10	0.3 ± 0.2	0.5 ± 0.2	0.0 ± 0.2	0.05 ± 0.1	0.06 ± 0.2	0.04 ± 0.2	4.2 ± 0.5	3.8 ± 0.9	4.6 ± 0.3
3 <sup>§</sup>	PLC Inhibitor	Agonists	18	-0.9 ± 0.2 <sup>#*</sup>	-1.3 ± 0.2 <sup>#</sup>	-0.6 ± 0.1 <sup>#</sup>	0.29 ± 0.1	0.20 ± 0.3	0.34 ± 0.1	3.5 ± 0.4	2.9 ± 0.2	3.9 ± 0.6
		Vehicle	25	0.1 ± 0.1	0.3 ± 0.1	-0.2 ± 0.2	-0.16 ± 0.1	-0.06 ± 0.2	-0.30 ± 0.2	4.4 ± 0.5	4.0 ± 0.6	5.1 ± 1.0
	AC Inhibitor	Agonists	37	-0.7 ± 0.1 <sup>#</sup>	-0.8 ± 0.2 <sup>#</sup>	-0.6 ± 0.1	0.00 ± 0.1	-0.08 ± 0.1	0.08 ± 0.1	3.5 ± 0.3	3.4 ± 0.4	3.6 ± 0.4
		Vehicle	6	-0.8 ± 0.2 <sup>†</sup>	-0.6 ± 0.2 <sup>†</sup>	-1.1 ± 0.2	-0.28 ± 0.2	-0.29 ± 0.3	-0.29 ± 0.3	4.0 ± 0.8	4.3 ± 1.2	3.5 ± 1.0
	PLC+AC Inhibitors	Agonists	7	-0.4 ± 0.2	-0.3 ± 0.3	-0.5 ± 0.2	-0.40 ± 0.3	-0.32 ± 0.4	-0.32 ± 0.4	4.4 ± 1.0	3.4 ± 0.6	5.8 ± 2.2
Vehicle		6	-0.9 ± 0.2 <sup>†</sup>	-0.9 ± 0.3 <sup>†</sup>	-0.9 ± 0.5	-0.20 ± 0.2	-0.15 ± 0.0	-0.15 ± 0.0	6.3 ± 0.6	6.3 ± 1.0	6.5 ± 0.4	
Agonists		7	-0.6 ± 0.3	-0.7 ± 0.6	-0.5 ± 0.2	-0.18 ± 0.1	-0.65 ± 0.2	0.05 ± 0.2	4.9 ± 1.1	5.1 ± 1.9	4.7 ± 0.9	
4a <sup>§</sup>	Vip <sup>cre/+</sup> ; PER2::LUC	Vehicle	6	-0.5 ± 0.5	-0.5 ± 0.3	-0.5 ± 1.1	-0.14 ± 0.3	-0.11 ± 0.5	0.00 ± 0.4	6.3 ± 2.1	8.3 ± 4.0 <sup>†</sup>	4.4 ± 1.6
		Agonists	9	0.6 ± 0.3 <sup>#*</sup>	0.0 ± 0.3	1.0 ± 0.4 <sup>#</sup>	0.08 ± 0.1 <sup>*</sup>	-0.16 ± 0.3	0.72 ± 0.2	6.3 ± 1.5 <sup>*</sup>	9.1 ± 2.6	4.0 ± 0.8
	Vip <sup>cre/cre</sup> ; PER2::LUC	Vehicle	10	0.3 ± 0.2	0.5 ± 0.2	0.0 ± 0.2	0.02 ± 0.2	0.21 ± 0.2	-0.16 ± 0.3	4.9 ± 0.8	3.8 ± 0.9	5.9 ± 1.3
		Agonists	18	-0.9 ± 0.1 <sup>#*</sup>	-1.3 ± 0.2 <sup>#</sup>	-0.6 ± 0.1	0.08 ± 0.1	-0.05 ± 0.1	0.16 ± 0.1	3.5 ± 0.4	2.9 ± 0.2	3.9 ± 0.6
		Vehicle	8	-0.2 ± 0.3	0.0 ± 0.4	-0.7 ± 0.2	-0.17 ± 0.1	0.00 ± 0.1	-0.44 ± 0.3	5.0 ± 0.6	5.6 ± 0.9	4.2 ± 0.2
Vip <sup>cre/cre</sup> ; PER2::LUC	Agonists	9	-0.3 ± 0.3	-0.5 ± 0.4	-0.4 ± 0.3	-0.04 ± 0.2 <sup>*</sup>	0.22 ± 0.2	-0.46 ± 0.2	3.3 ± 0.4	3.5 ± 0.5	2.6 ± 0.9	
	Vehicle	7	-0.2 ± 0.2	-0.0 ± 0.2	-0.5 ± 0.4	-0.06 ± 0.2	-0.06 ± 0.2	-0.06 ± 0.1	6.5 ± 1.1	6.4 ± 1.3	6.7 ± 2.9	
4b <sup>§</sup>	VPAC2 Antagonist	Agonists	9	-0.2 ± 0.2	0.0 ± 0.3	-0.4 ± 0.3	0.03 ± 0.1	0.20 ± 0.1	-0.19 ± 0.2	4.8 ± 0.8	5.5 ± 1.6	4.2 ± 0.4
		Vehicle	22	0.1 ± 0.1	0.3 ± 0.1	-0.1 ± 0.1	-0.17 ± 0.1	-0.06 ± 0.2	-0.36 ± 0.2	3.3 ± 0.5	4.0 ± 0.6	4.9 ± 1.1
	VPAC2 Vehicle	Agonists	36	-0.7 ± 0.1 <sup>#</sup>	-0.8 ± 0.2 <sup>#</sup>	-0.6 ± 0.1 <sup>#</sup>	-0.02 ± 0.1	-0.08 ± 0.1	0.05 ± 0.1 <sup>#</sup>	4.5 ± 0.3	3.4 ± 0.4	3.6 ± 0.4
		Vehicle	6	-0.4 ± 0.2	0.0 ± 0.2	-0.7 ± 0.1	-0.48 ± 0.1	-0.56 ± 0.2	-0.41 ± 0.1	3.0 ± 0.3	3.0 ± 0.6	3.0 ± 0.4
Agonists	6	-0.3 ± 0.3	0.1 ± 0.2	-0.6 ± 0.1	-0.52 ± 0.1	-0.36 ± 0.1	-0.68 ± 0.3	4.7 ± 1.3	5.2 ± 2.5	4.2 ± 1.4		

<sup>§</sup>1a Phase Shift FF ANOVA, Concentration:  $F(4,46) = 10.7, p < 0.001$ , Sex:  $F(1,46) = 0.5, p > 0.4$ , Concentration\*Sex:  $F(4,46) = 3.2, p = 0.02$ , Period Difference FF ANOVA, Concentration:  $F(4,46) = 2.6, p = 0.05$ , Sex:  $F(1,46) = 0.4, p > 0.5$ , Concentration\*Sex:  $F(4,46) = 1.4, p > 0.2$ , Damping FF ANOVA, Concentration:  $F(4,44) = 1.4, p > 0.2$ , Sex:  $F(1,44) = 0.0, p > 0.8$ , Concentration\*Sex:  $F(4,44) = 0.9, p > 0.4$

<sup>§</sup>1b Phase Shift FF ANOVA, Drug Group:  $F(2,36) = 18.4, p < 0.001$ , Sex:  $F(1,36) = 0.8, p > 0.3$ , Drug Group\*Sex:  $F(2,36) = 3.4, p = 0.05$ , Period Difference FF ANOVA, Drug Group:  $F(2,36) = 1.9, p > 0.1$ , Sex:  $F(1,36) = 3.8, p = 0.06$ , Drug Group\*Sex:  $F(2,36) = 3.6, p = 0.04$ , Damping FF ANOVA, Drug Group:  $F(2,35) = 2.4, p = 0.1$ , Sex:  $F(1,35) = 4.5, p = 0.04$ , Drug Group\*Sex:  $F(2,35) = 0.4, p > 0.6$

<sup>§</sup>1c Phase Shift FF ANOVA, V1 Agonist:  $F(3,76) = 6.3, p < 0.001$ , Sex:  $F(1,76) = 0.1, p > 0.7$ , V1 Agonist\*Sex:  $F(3,76) = 2.1, p = 0.1$ , Period Difference FF ANOVA, V1 Agonist:  $F(3,73) = 1.4, p > 0.2$ , Sex:  $F(1,73) = 0.2, p > 0.6$ , V1 Agonist\*Sex:  $F(3,73) = 0.5, p > 0.6$ , Damping FF ANOVA, V1 Agonist:  $F(3,68) = 2.1, p > 0.1$ , Sex:  $F(1,68) = 2.4, p > 0.1$ , V1 Agonist\*Sex:  $F(3,68) = 0.2, p > 0.9$

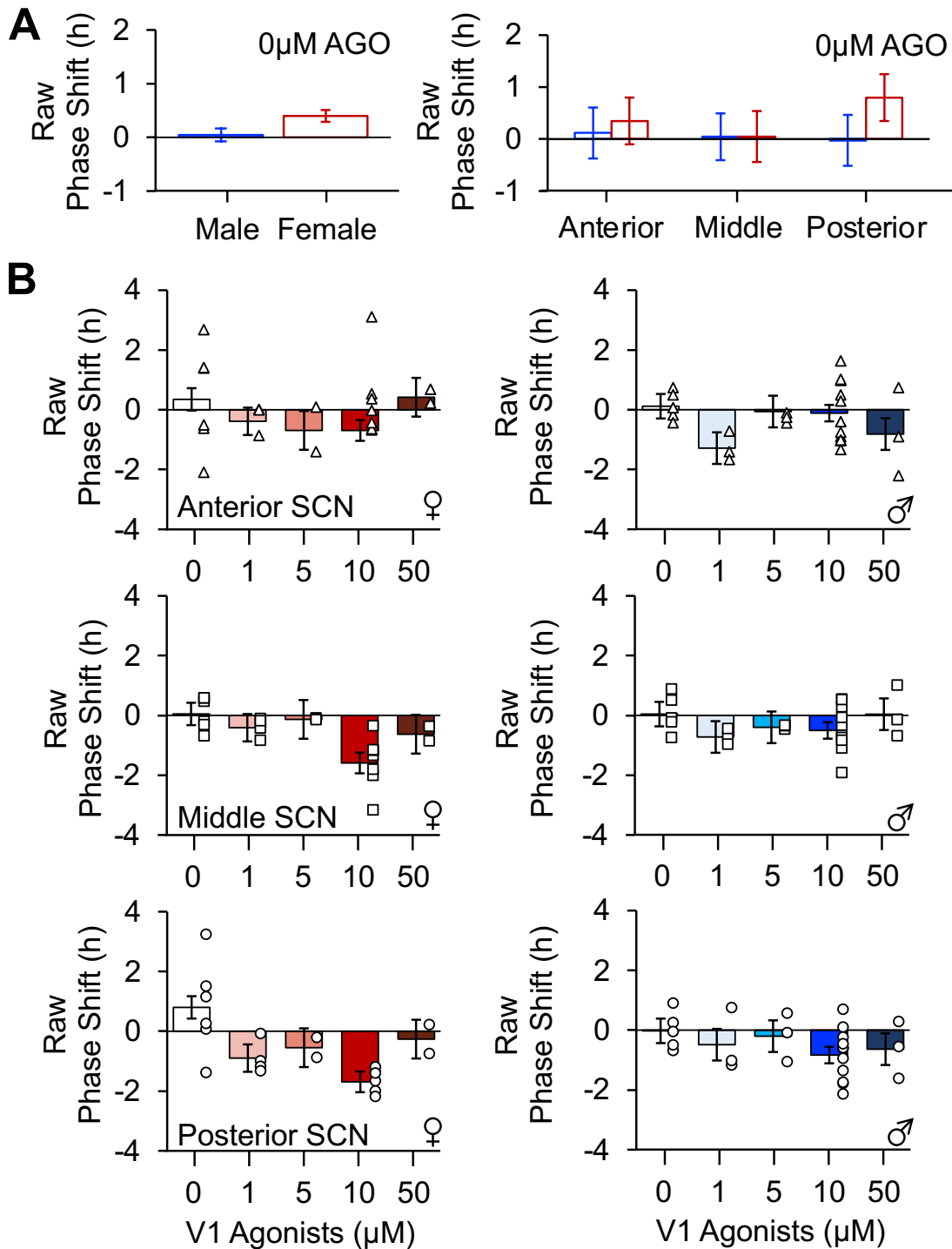
<sup>§</sup>2 Phase Shift FF ANOVA, Drug Group:  $F(1,80) = 18.4, p < 0.001$ , Sex:  $F(1,80) = 1.4, p > 0.2$ , Drug Group\*Sex:  $F(1,80) = 2.4, p > 0.1$ , CT:  $F(3,80) = 11.9, p < 0.001$ , Drug Group\*CT:  $F(3,80) = 9.8, p < 0.001$ , Sex\*CT:  $F(3,80) = 1.1, p > 0.3$ , Drug Group\*Sex\*CT:  $F(3,80) = 2.6, p = 0.06$ , Period Difference FF ANOVA, Drug Group:  $F(1,80) = 1.3, p > 0.2$ , Sex:  $F(1,80) = 4.9, p = 0.03$ , Drug Group\*Sex:  $F(1,80) = 0.1, p > 0.7$ , CT:  $F(3,80) = 16.7, p < 0.001$ , Drug Group\*CT:  $F(3,80) = 0.5, p > 0.7$ , Sex\*CT:  $F(3,80) = 2.7, p = 0.05$ , Drug Group\*Sex\*CT:  $F(3,80) = 2.2, p = 0.09$ , Damping FF ANOVA, Drug Group:  $F(1,77) = 0.4, p > 0.5$ , Sex:  $F(1,77) = 2.8, p = 0.1$ , Drug Group\*Sex:  $F(1,77) = 1.9, p > 0.1$ , CT:  $F(3,77) = 0.7, p > 0.5$ , Drug Group\*CT:  $F(3,77) = 3.0, p = 0.04$ , Sex\*CT:  $F(3,77) = 0.3, p > 0.8$ , Drug Group\*Sex\*CT:  $F(3,77) = 0.2, p > 0.9$

<sup>§</sup>3 Phase Shift FF ANOVA, V1 Agonist:  $F(1,98) = 2.1, p > 0.1$ , Inhibitor:  $F(3,98) = 3.6, p = 0.02$ , V1 Agonist\*Inhibitor:  $F(3,98) = 8.2, p < 0.001$ , Sex:  $F(1,98) = 0.0, p > 0.9$ , V1 Agonist\*Sex:  $F(1,198) = 2.7, p > 0.1$ , Inhibitor\*Sex:  $F(3,98) = 1.2, p > 0.3$ , V1 Agonist\*Inhibitor\*Sex:  $F(3,98) = 0.3, p > 0.8$ , Period Difference FF ANOVA, V1 Agonist:  $F(1,98) = 0.1, p > 0.7$ , Inhibitor:  $F(3,98) = 1.7, p > 0.1$ , V1 Agonist\*Inhibitor:  $F(3,98) = 0.9, p > 0.4$ , Sex:  $F(1,98) = 2.4, p > 0.1$ , V1 Agonist\*Sex:  $F(1,98) = 4.2, p = 0.04$ , Inhibitor\*Sex:  $F(3,98) = 1.1, p > 0.3$ , V1 Agonist\*Inhibitor\*Sex:  $F(3,98) = 0.3, p > 0.8$ , Damping FF ANOVA, V1 Agonist:  $F(1,96) = 0.4, p > 0.5$ , Inhibitor:  $F(3,96) = 4.3, p = 0.01$ , V1 Agonist\*Inhibitor:  $F(3,96) = 0.7, p > 0.5$ , Sex:  $F(1,96) = 1.5, p > 0.2$ , V1 Agonist\*Sex:  $F(1,96) = 0.0, p > 0.9$ , Inhibitor\*Sex:  $F(3,96) = 4.0, p = 0.01$ , V1 Agonist\*Inhibitor\*Sex:  $F(3,96) = 0.6, p > 0.6$

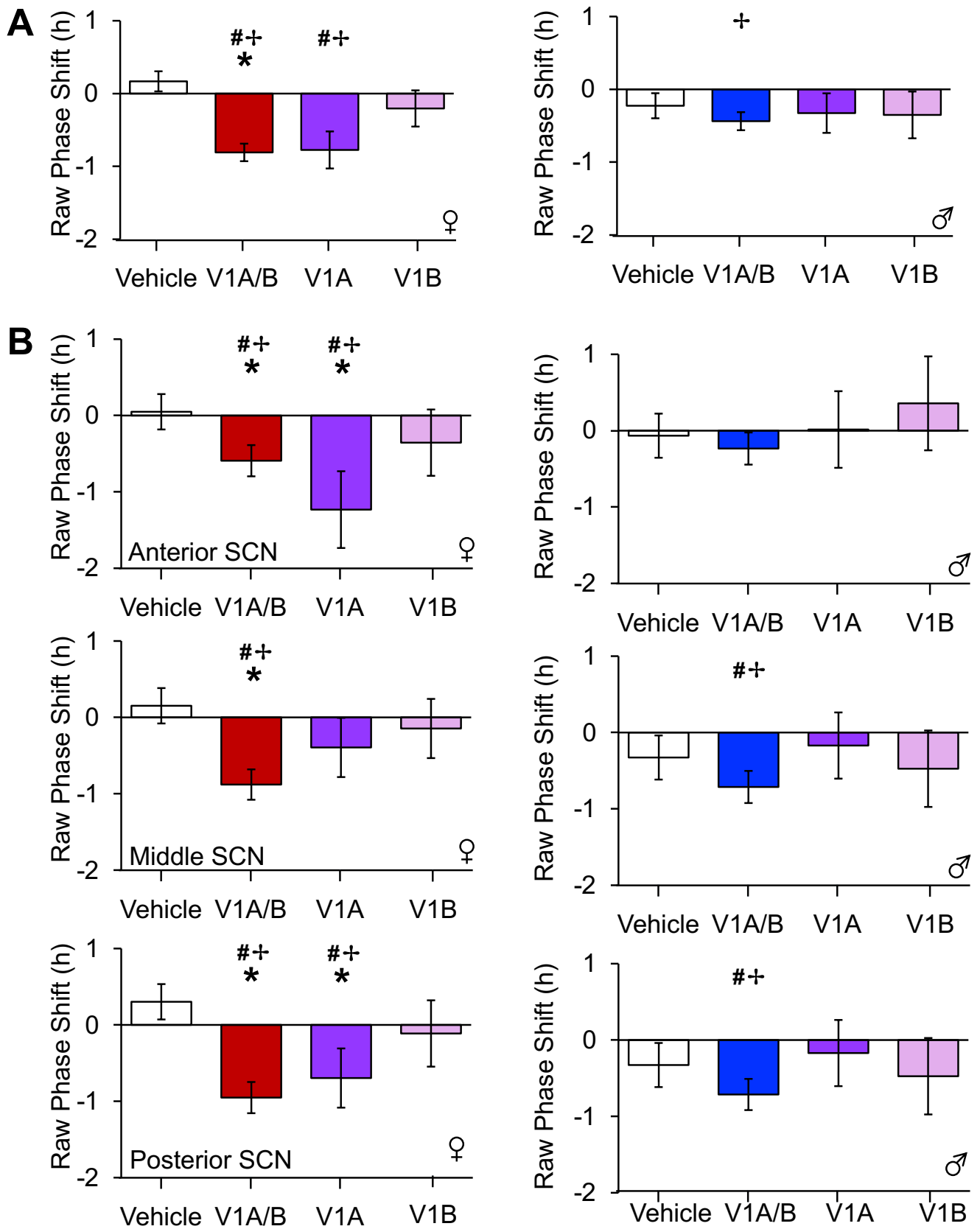
<sup>§</sup>4a Phase Shift FF ANOVA, Genotype:  $F(2,59) = 0.2, p > 0.8$ , Drug Group:  $F(1,59) = 4.2, p = 0.05$ , Genotype\*Drug Group:  $F(2,59) = 6.6, p < 0.005$ , Sex:  $F(1,59) = 0.8, p > 0.3$ , Genotype\*Sex:  $F(2,59) = 0.7, p > 0.4$ , Drug Group\*Sex:  $F(1,59) = 4.4, p = 0.04$ , Genotype\*Drug Group\*Sex:  $F(2,59) = 1.0, p > 0.3$ , Period Difference FF ANOVA, Genotype:  $F(2,59) = 1.4, p > 0.2$ , Drug Group:  $F(1,59) = 0.4, p > 0.5$ , Genotype\*Drug Group:  $F(2,59) = 0.0, p > 0.9$ , Sex:  $F(1,59) = 6.7, p = 0.01$ , Genotype\*Sex:  $F(2,59) = 1.8, p > 0.1$ , Drug Group\*Sex:  $F(1,59) = 0.0, p > 0.9$ , Genotype\*Drug Group\*Sex:  $F(2,59) = 2.3, p = 0.11$ , Damping FF ANOVA, Genotype:  $F(2,55) = 3.2, p = 0.05$ , Drug Group:  $F(1,55) = 8.0, p = 0.01$ , Genotype\*Drug Group:  $F(2,55) = 0.0, p > 0.9$ , Sex:  $F(1,55) = 0.0, p > 0.9$ , Genotype\*Sex:  $F(2,55) = 2.3, p = 0.11$ , Drug Group\*Sex:  $F(1,55) = 0.4, p > 0.5$ , Genotype\*Drug Group\*Sex:  $F(2,55) = 0.2, p > 0.7$

<sup>§</sup>4b Phase Shift FF ANOVA, VPAC2 Antagonist:  $F(1,69) = 0.0, p > 0.9$ , V1 Agonist:  $F(1,69) = 3.8, p = 0.06$ , VPAC2 Antagonist\*V1 Agonist:  $F(1,69) = 6.3, p = 0.01$ , Sex:  $F(1,69) = 5.2, p = 0.03$ , VPAC2 Antagonist\*Sex:  $F(1,69) = 3.8, p = 0.06$ , V1 Agonist\*Sex:  $F(1,69) = 0.8, p > 0.3$ , VPAC2 Antagonist\*V1 Agonist\*Sex:  $F(1,69) = 0.8, p > 0.3$ , Period Difference FF ANOVA, VPAC2 Antagonist:  $F(1,69) = 6.7, p = 0.01$ , V1 Agonist:  $F(1,69) = 0.3, p > 0.6$ , VPAC2 Antagonist\*V1 Agonist:  $F(1,69) = 0.6, p > 0.4$ , Sex:  $F(1,69) = 0.3, p > 0.5$ , VPAC2 Antagonist\*Sex:  $F(1,69) = 0.0, p > 0.9$ , V1 Agonist\*Sex:  $F(1,69) = 0.0, p > 0.9$ , VPAC2 Antagonist\*V1 Agonist\*Sex:  $F(1,69) = 2.2, p > 0.1$ , Damping FF ANOVA, VPAC2 Antagonist:  $F(1,69) = 0.0, p > 0.8$ , V1 Agonist:  $F(1,69) = 0.3, p > 0.5$ , VPAC2 Antagonist\*V1 Agonist:  $F(1,69) = 3.8, p = 0.06$ , Sex:  $F(1,69) = 0.0, p > 0.9$ , VPAC2 Antagonist\*Sex:  $F(1,69) = 0.5, p > 0.4$ , V1 Agonist\*Sex:  $F(1,69) = 0.5, p > 0.5$ , VPAC2 Antagonist\*V1 Agonist\*Sex:  $F(1,69) = 0.0, p > 0.8$

\* Sex difference,  $p < 0.05$ . # Agonist different from Vehicle,  $p < 0.05$ . † Inhibitor difference,  $p < 0.05$

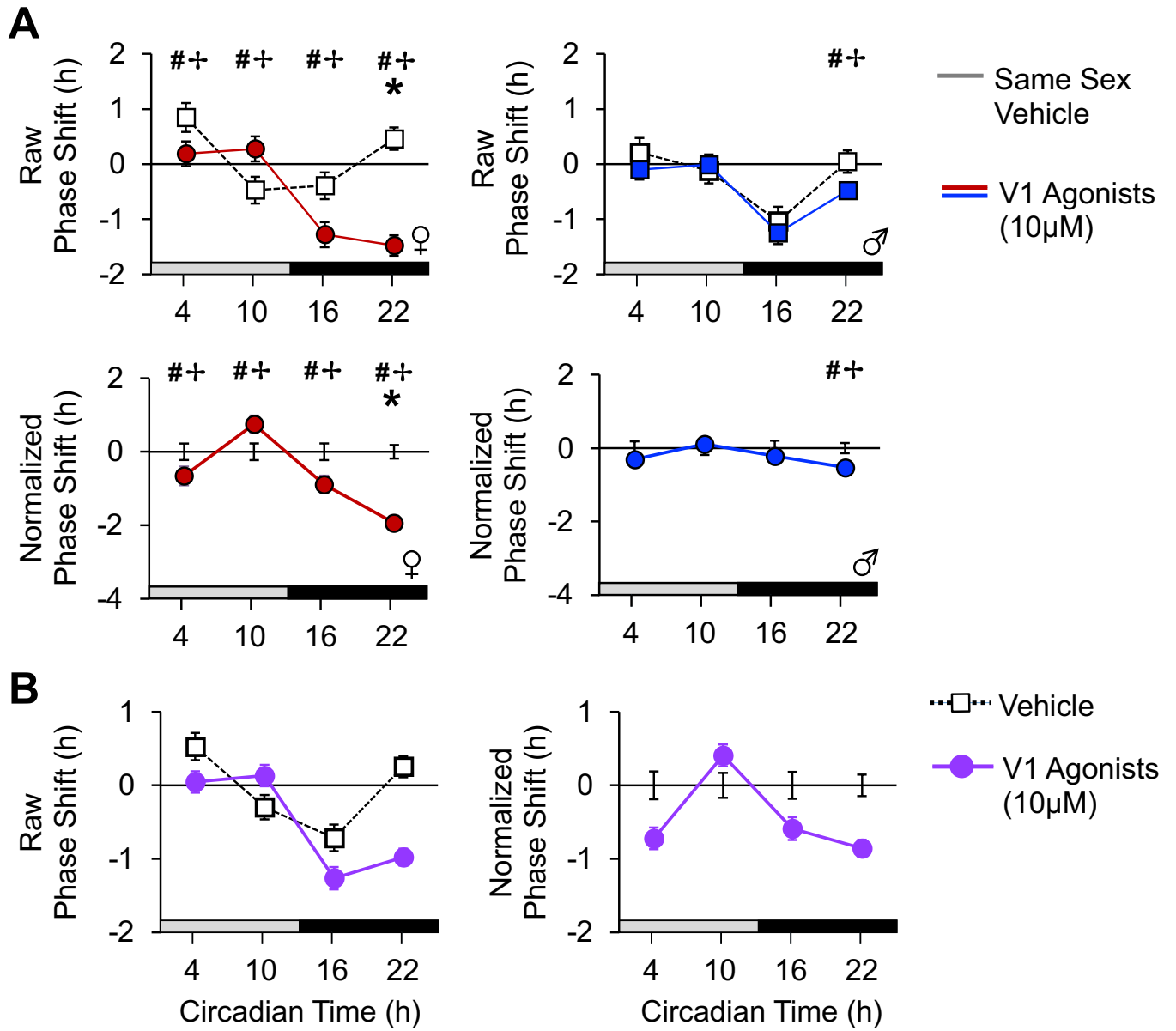


**Supplemental Figure S1. V1A/B receptor agonists reset PER2::LUC rhythms in a dose- and sex-dependent manner.** A. Phase shifting responses to vehicle administration. B. Phase shifting responses to vehicle and V1A/B agonist treatment divided by sex and SCN slice position. Scatterplot indicates data for individual samples. # Different from Vehicle. Estimated Marginal Means Contrasts:  $p < 0.05$ . + Different from zero, Single sample t-test:  $p < 0.05$ . \* Different by sex, Estimated Marginal Means Contrasts:  $p < 0.05$ .

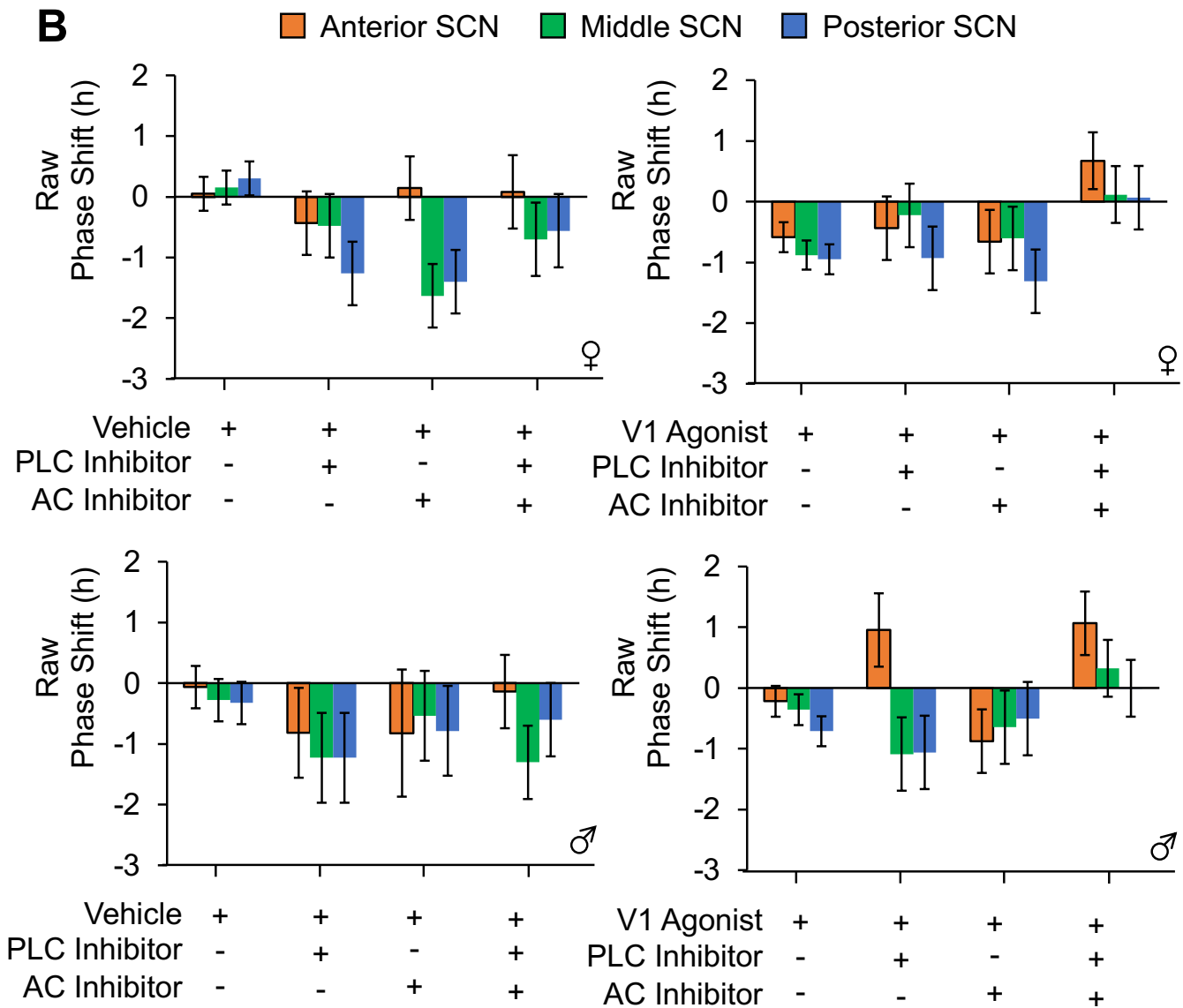
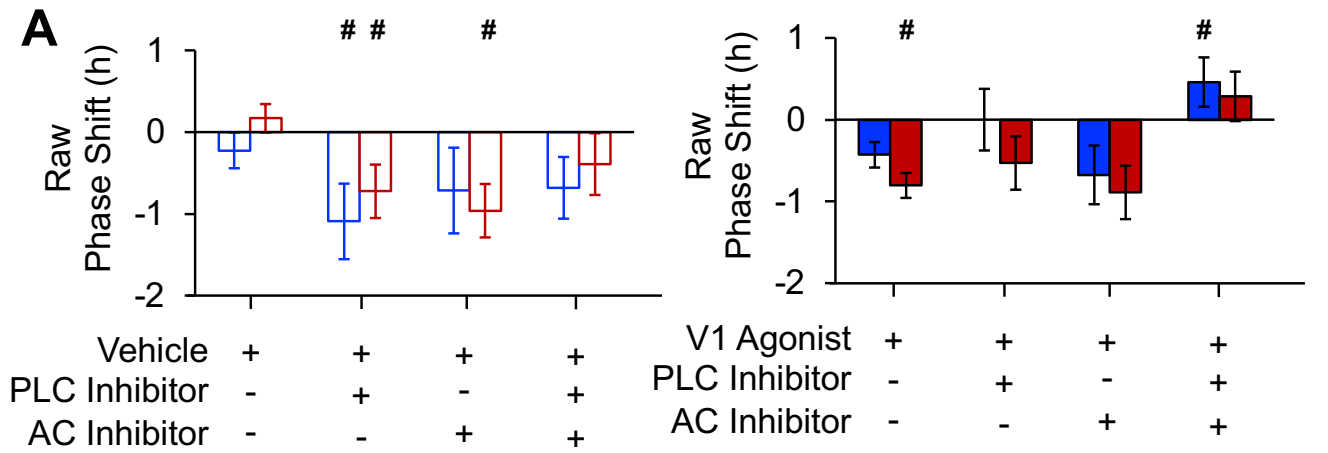


**Supplemental Figure S2. SCN resetting to single V1 agonists divided by sex position.**

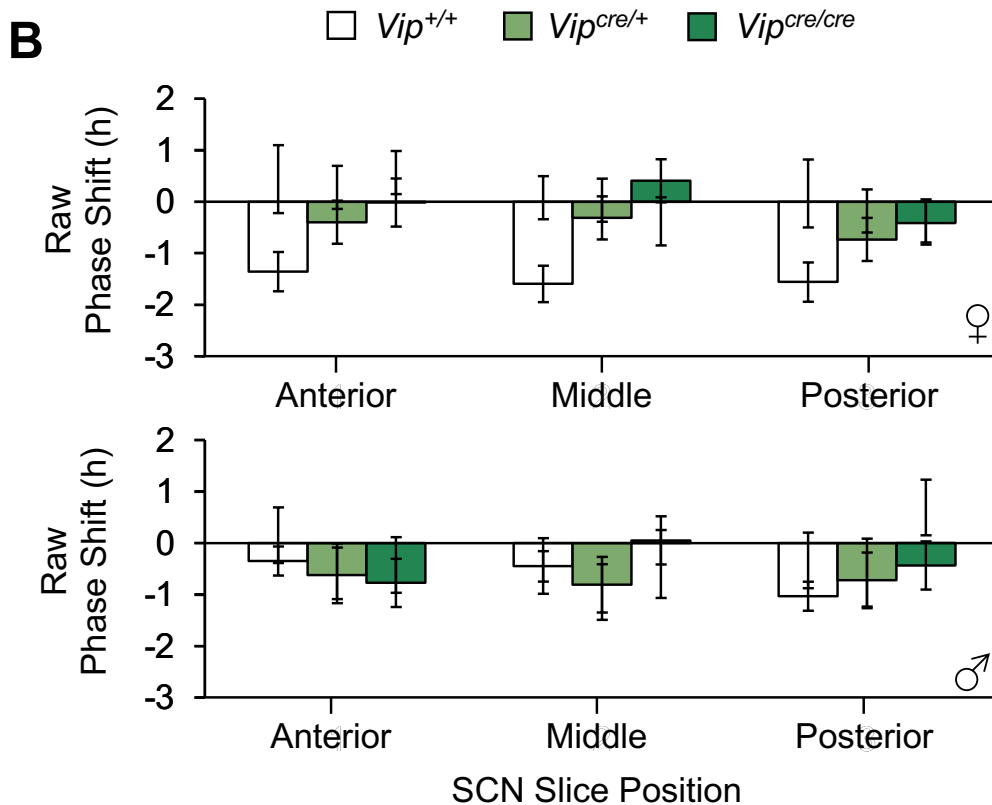
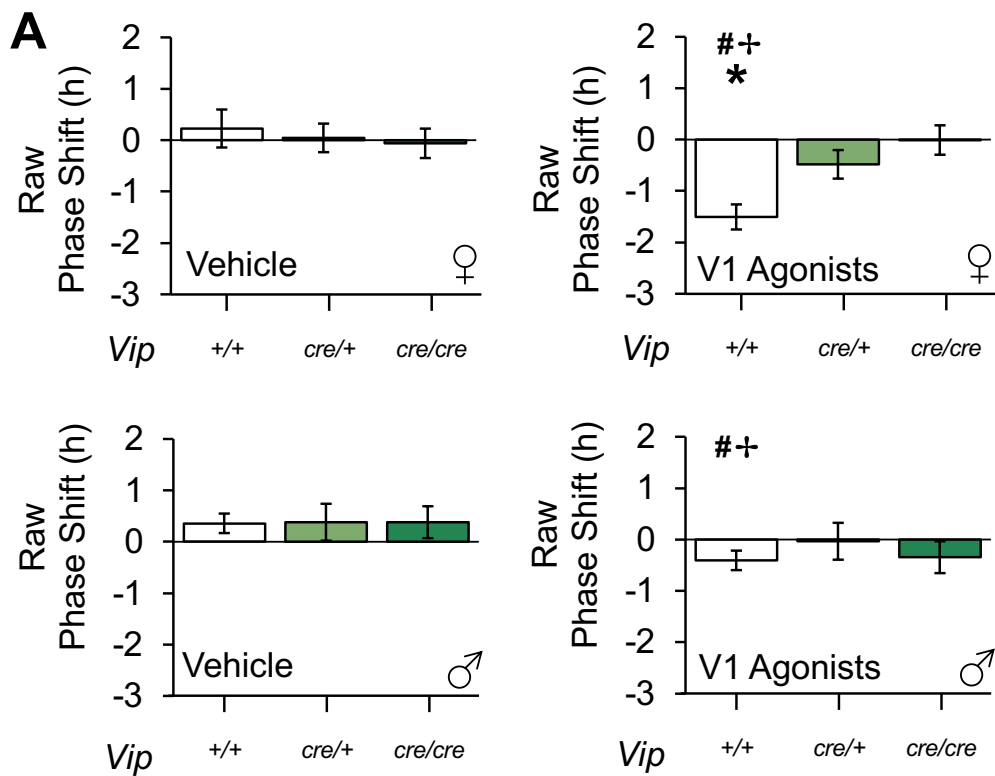
# Different from Vehicle. Estimated Marginal Means Contrasts:  $p < 0.05$ . + Different from zero, Single sample t-test:  $p < 0.05$ . \* Different by sex, Estimated Marginal Means Contrasts:  $p < 0.05$ .



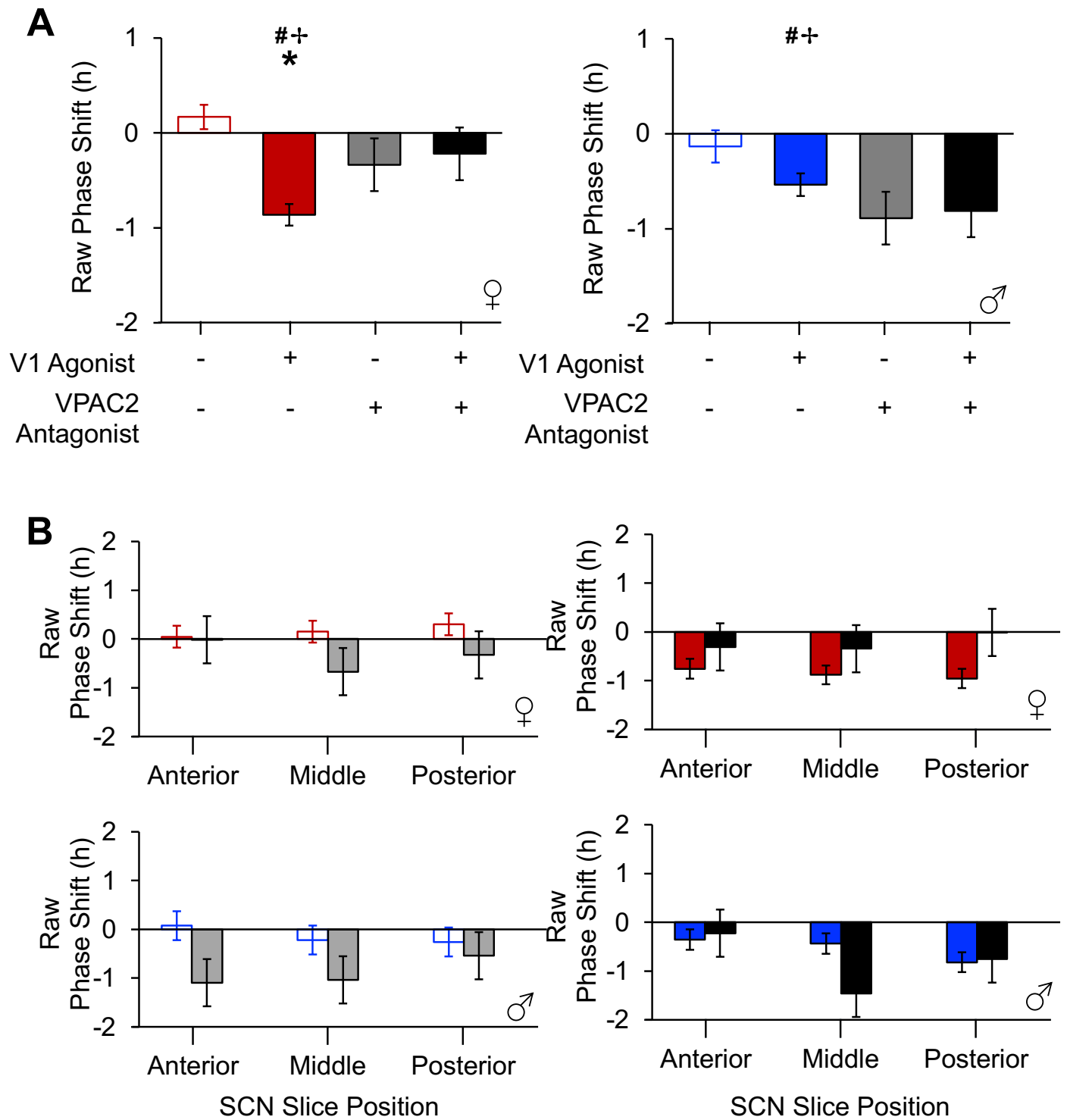
**Supplemental Figure S3. SCN resetting to V1A/B agonists at different circadian times.** # Different from Vehicle. Estimated Marginal Means Contrasts:  $p < 0.05$ . + Different from zero, Single sample t-test:  $p < 0.05$ . \* Different by sex, Estimated Marginal Means Contrasts:  $p < 0.05$ .



**Supplemental Figure S4. SCN resetting to PLC, AC, and V1 agonists.** # Different from Vehicle. Estimated Marginal Means Contrasts:  $p < 0.05$ . + Different from zero, Single sample t-test:  $p < 0.05$ . \* Different by sex, Estimated Marginal Means Contrasts:  $p < 0.05$ .



**Supplemental Figure S5. VIP deficiency blocks V1A/B-induced SCN resetting**  
 # Different from Vehicle. Estimated Marginal Means Contrasts:  $p < 0.05$ . + Different from zero, Single sample t-test:  $p < 0.05$ . \* Different by sex, Estimated Marginal Means Contrasts:  $p < 0.05$ .



**Supplemental Figure S6. VPAC2 antagonist blocks V1-induced resetting.** A-B. VPAC2 antagonist co-administration blocked V1-induced SCN resetting. \* Different by sex, Estimated Marginal Means Contrasts:  $p < 0.05$ . + Different from zero, Single sample t-test:  $p < 0.05$  (symbols color coded in S2B based on Antagonist).