

TITLE: NOREPINEPHRINE AS A MEMORY RESET SIGNAL

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SUPPLEMENTAL TABLES

Table S1. *Number of animals in each experiment.*

Exp	Behavioral Paradigm	Group	n	Figure
Pilot	DNMP	--	12	S1A-S1C
1	DNMP	ISO	20	1D-1I; S1D-H; S2A-I
1	DNMP	PRO	20	1D-1I; S1D-H; S2A-I
2	EPM	VEH	5	2A-2F
2	EPM	ISO	5	2A-2F
2	EPM	PRO	5	2A-2F
3	BARNES	VEH-VEH	6	3C-3J; 4A-C; S3A-J; S5A-B
3	BARNES	VEH-ISO	5	3C-3J; 4A-C; S3A-J; S5A-B
3	BARNES	PRO-VEH	3	3C-3J; 4A-C; S3A-J; S5A-B
3	BARNES	PRO-ISO	3	3C-3J; 4A-C; S3A-J; S5A-B
3	BARNES	VEH-VEH-ISO	3	4D-3L; S5C

Note: DNMP = Delayed Non-Match to Position; EPM = Elevated Plus Maze; BARNES = Barnes Maze; ISO = Isoproterenol; PRO = Propranolol; VEH = Vehicle (Saline).

Table S2. *List of studies used to determine drug doses*

Reference	Drug	Concentration (mM)	Concentration (µg/µL)	Volume Infused (per side/µL)	Infusion Rate (µL/min)	Duration (min)	Total Mass (per side/µg)	Target	Effects
Geyer & Masten, 1989	L-isoproterenol hydrochloride	0.4000	0.1000	20.0	0.3330	60.0	2.0000	DG	increased exploration
Geyer & Masten, 1989	L-isoproterenol hydrochloride	1.2000	0.3000	20.0	0.3330	60.0	6.0000	DG	increased exploration
Sun et al., 2005	L-isoproterenol hydrochloride	400.0000	99.088	2.0	0.0667	30.0	198.1760	CA1	spatial memory impairments
Qi et al., 2008	L-isoproterenol hydrochloride	40.3682	10.0000	1.0	0.5000	2.0	10.0000	CA1	impaired retrieval
Alsene et al., 2011	L-isoproterenol hydrochloride	12.1104	3.0000	0.5	0.5000	1.0	1.5000	DG & CA1	no effect
Alsene et al., 2011	L-isoproterenol hydrochloride	40.3682	10.0000	0.5	0.5000	1.0	5.0000	DG & CA1	no effect
Alsene et al., 2011	L-isoproterenol hydrochloride	121.1045	30.0000	0.5	0.5000	1.0	15.0000	DG & CA1	no effect
Lethbridge, Walling, & Harley, 2014	L-isoproterenol hydrochloride	0.0001	0.000247	1.0	0.0800	12.0	0.000247	DG	induced LTD
Lethbridge, Walling, & Harley, 2014	L-isoproterenol hydrochloride	0.0010	0.000247	1.0	0.0800	12.0	0.000247	DG	no effect
Lethbridge, Walling, & Harley, 2014	L-isoproterenol hydrochloride	0.0100	0.00247	1.0	0.0800	12.0	0.00247	DG	no effect
Lethbridge, Walling, & Harley, 2014	L-isoproterenol hydrochloride	0.1000	0.0247	1.0	0.0800	12.0	0.0247	DG	induced LTP
Hansen & Manahan-Vaughan, 2015	L-isoproterenol hydrochloride	16.1473	4.0000	5.0	1.0000	5.0	20.0000	ICV	strengthened LTP
Garrido-Zinn et al., 2016	L-isoproterenol hydrochloride	80.7363	20.0000	0.5	0.5000	1.0	10.0000	BLA	no effect
Garrido-Zinn et al., 2016	L-isoproterenol hydrochloride	40.3682	10.0000	1.0	1.0000	1.0	10.0000	CA1	impaired retrieval
Current Study	isoproterenol-bitartrate	47.3350	10.0000	0.5	0.5000	1.0	5.0000	DG	impaired spatial memory
Ji et al., 2003	propranolol hydrochloride	16.9027	5.0000	1.0	0.5000	2.0	5.0000	CA1	impaired consolidation
Chai et al., 2014	propranolol hydrochloride	33.8055	10.0000	0.5	0.5000	1.0	5.0000	CA1	blocked NE-facilitated memory enhancements
Hatfield & McGaugh, 1999	propranolol hydrochloride	5.0708	1.5000	0.2	0.5000	0.4	0.3000	BLA	spatial memory impairments
Hansen & Manahan-Vaughan, 2015	propranolol hydrochloride	1.3522	0.4000	5.0	1.0000	5.0	2.0000	ICV	LTP impairment
Straube et al., 2003	propranolol hydrochloride	0.0068	0.0020	5.0	1.2500	4.0	0.009998	ICV	blocked novelty induced LTP reinforcement in DG
Walling & Harley, 2004	propranolol hydrochloride	20.2840	6.0000	5.0	1.0000	5.0	30.0000	ICV	blocked LC-GLUT induced plasticity
Qi et al., 2008	propranolol hydrochloride	50.7082	15.0000	1.0	0.5000	2.0	15.0000	CA1	did not impair retrieval
Barseganyan, McGaugh, & Roozendaal, 2014	propranolol hydrochloride	1.6903	0.5000	0.2	0.4000	0.5	0.1000	BLA	no effect
Barseganyan, McGaugh, & Roozendaal, 2014	propranolol hydrochloride	5.0710	1.5000	0.2	0.4000	0.5	0.3000	BLA	diminished NE-facilitated memory enhancements
Current Study	propranolol hydrochloride	10.1420	3.0000	0.5	0.5000	1.0	1.5000	DG	no effect

Note: DG = Dentate Gyrus; CA1= Cornu Ammonis; BLA = Basolateral Amygdala; ICV = Intracerebroventricular; LC = Locus Coeruleus; NE = Norepinephrine; GLUT = Glutamate; LTP = Long Term Potentiation; LTD = Long Term Depression. All hippocampal regions (DG & CA1) were dorsally targeted. All injections were bilateral except ICV injections.

Table S3. *Combinations of arm separations used for acquisition and washout.*

5 CW		5 CCW		2 CW		2 CCW		Day
Sample Arm	Choice Arm	Sample Arm	Choice Arm	Sample Arm	Choice Arm	Sample Arm	Choice Arm	
2	7	11	6	3	5	12	10	A1
11	4	8	3	7	9	6	4	A2
6	11	9	4	12	2	5	3	A3
7	12	10	5	6	8	11	9	A4
9	2	4	11	8	10	7	5	A5
3	8	12	7	9	11	4	2	A6
12	5	3	10	5	7	2	12	W1
4	9	7	2	10	12	9	7	W2
10	3	5	12	4	6	10	8	W3
5	10	2	9	2	4	8	6	W4

Note: Animals were tested with an arm separation of 2 or 5 counterbalanced for clockwise (grey) and counter-clockwise (white) directions. The order of testing is shown in Table S5.

Table S4. *Testing Schedule: Order of S2 and S5 trials during acquisition and washout.*

Rat	Trial 1	Trial 2	Trial 3	Trial 4
1	5R	2L	2R	5L
2	5R	2L	5L	2R
3	5R	2R	2L	5L
4	5R	2R	5L	2L
5	5R	5L	2R	2L
6	5R	5L	2L	2R
7	5L	2L	2R	5R
8	5L	2L	5R	2R
9	5L	2R	2L	5R
10	5L	2R	5R	2L
11	5L	5R	2L	2R
12	5L	5R	2R	2L
13	2R	2L	5R	5L
14	2R	2L	5L	5R
15	2R	5L	2L	5R
16	2R	5L	5R	2L
17	2R	5R	2L	5L
18	2R	5R	5L	2L
19	2L	2R	5R	5L
20	2L	2R	5R	5L
21	2L	5R	2R	5L
22	2L	5R	5L	2R
23	2L	5L	2R	5R
24	2L	5L	5R	2R

Note: Rats received 4 trials / day. R = Clockwise, L = Counter-clockwise

Table S5. *Balanced Latin Square Design Used for Testing Schedule*

Rat	Test 1	Test 2	Test 3	Test 4	Pattern
1	PS5	PC5	PS2	PC2	DCBA
2	PC5	PS2	PC2	PS5	CBAD
3	PS2	PC2	PS5	PC5	BADC
4	PC2	PS5	PC5	PS2	ADCB
5	PC2	PS2	PC5	PS5	ABCD
6	PS2	PC5	PS5	PC2	BCDA
7	PC5	PS5	PC2	PS2	CDAB
8	PS5	PC2	PS2	PC5	DABC
9	PS2	PS5	PC2	PC5	BDAC
10	PS5	PC2	PC5	PS2	DACB
11	PC2	PC5	PS2	PS5	ACDB
12	PC5	PS2	PS5	PC2	CBDA
13	PC5	PC2	PS5	PS2	CADB
14	PC2	PS5	PS2	PC5	ADBC
15	PS5	PS2	PC5	PC2	DBCA
16	PS2	PC5	PC2	PS5	BCAD
17	PC5	PS5	PS2	PC2	CDBA
18	PS5	PS2	PC2	PC5	DBAC
19	PS2	PC2	PC5	PS5	BACD
20	PC2	PC5	PS5	PS2	ACDB

Note: PC2=A; PS2=B; PC5=C; PS5=D.

Infusions made “Pre-Choice” = PC, infusions made “Pre-Sample” = PS.

Animals were tested with an arm separation of 2 or 5.

Table S6. *Experiment 1 (DNMP) design across the four test days*

Between-Subject Group	Within-Subject Infusion Time	Within-Subject Arm Separation	Within-Subject Trial
ISO	PS	S2	HAB-BASE-TEST
ISO	PS	S5	HAB-BASE-TEST
ISO	PC	S2	HAB-BASE-TEST
ISO	PC	S5	HAB-BASE-TEST
PRO	PS	S2	HAB-BASE-TEST
PRO	PS	S5	HAB-BASE-TEST
PRO	PC	S2	HAB-BASE-TEST
PRO	PC	S5	HAB-BASE-TEST

Note: ISO = Isoproterenol; PRO = Propranolol; PS = infusions made Pre-Sample. PC = infusions made Pre-Choice. Animals were tested with an arm separation of 2 (S2) or 5 (S5). HAB = habituation trial; BASE = baseline trial; TEST = test trial.

Table S7. *Cardinal direction rat was facing at the start of the trial.*

Direction	Number of Trials	Percentage of Trials (%)
North	236	27.76
West	227	26.71
South	191	22.47
East	196	23.06

Note: Total number of trials (not including habituation which was not videotaped) = 850.