

Supplementary Information for

Ventromedial prefrontal area 14 provides opposing regulation of threat and reward-elicited responses in the common marmoset

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Figure S1. Rise in systolic blood pressure during the US relative to the CS of the acquisition session trials during the extinction blocks. Pre-snake indicates the period during which an empty compartment is revealed prior to the snake being inserted (US-). A two-way ANOVA (US pair x treatment block) revealed a significant effect of US pair only ($F_{(3,18)}$ =4.06, p=0.023). There was no significant difference between treatment blocks (treatment block effect: $F_{(2,12)}$ =2.02, p=0.176; treatment block x US pair interaction: F<1). Data are displayed as systolic blood pressure (SysBP) means ± SEM (n=7), with significance values indicated as p<0.05*.



Figure S2. Evidence for behavioural and cardiovascular threat acquisition. Figure compares behavioral (A) and systolic blood pressure (SysBP; B) responses during the CS before and after snake presentation (Pre-snake and Post-snake respectively) with data normalized to the Pre-snake period. A linear mixed effects model analysis on vigilant scanning behavior (A; phase x treatment) revealed an effect of phase ($F_{(1,32)}$ =21.5, p<0.001) indicating successful acquisition of conditioning to the CS. Similar successful conditioning was observed for sysBP (B) as a two-way ANOVA (phase x treatment) revealed an effect of phase only ($F_{(1,6)}$ =18, p=0.0082). For CS-directed SysBP (C; CS minus baseline), no significant effects were observed using a two-way ANOVA (phase x treatment), due to high variation during the post-snake period. Data are displayed as means ± SEM (n=7), with comparison significance values of p<0.05* and p<0.001***.



Figure S3. Area 14 over-activation and inactivation effects on appetitive conditioning CS- and CS+ trials. A. CSdirected behavioral arousal for the CS- and CS+ trials is displayed separately, with a one-way ANOVA on the responses to the CS+ revealing a significant effect of treatment ($F_{(2,12)}$ =20.26, p<0.001) with post-hoc multiple comparisons revealing a blunted DHK response (p=0.009) and enhanced Mus-Bac response (p=0.007) compared to saline, as well as a clear difference between DHK and Mus-Bac (p<0.001). Friedman's test for non-parametric data on CS- responses revealed a significant treatment effect (χ^2 =11.19, p=0.001), with a significant reduction by DHK to both saline (p=0.033) and Mus-Bac (p=0.006). **B.** Breakdown of CS-directed blood pressure changes to the CS- and CS+ trials show a significant effect of treatment (One-way ANOVA, $F_{(2,10)}$ =4.133, p=0.049) with the posthoc comparisons revealing a difference between DHK and Mus-Bac only (p=0.017). The same tests also revealed a significant difference in the response to the CS- ($F_{(2,10)}$ =6.282, p=0.0171), once again attributable to a difference between DHK and Mus-Bac (p=0.006). Data are displayed as means ± SEM (n=6 for SysBP, n=7 for behavior), with posthoc significance values indicated as p<0.05*, p<0.01** and p<0.001***.

	Rostral Caudal							
Subject	\otimes	\bigcirc		Δ	\bigtriangledown	0	\diamond	Mean
IA Dist.	+16.00	+16.00	+15.50	+15.00	+15.00	+14.50	+14.30	
Total infusions	24	20	24	26	23	17	20	22
Human Intruder Test – EFA Score								
Saline	0.04	1.11	-0.03	-1.82	0.00	-0.50	-0.19	-0.20
Mus-Bac	0.03	1.56	-0.26	-1.63	-0.57	0.13	-0.38	-0.16
DHK	0.40	1.40	0.19	-0.37	1.54	0.46	0.77	0.63
MB-Sal	-0.01	0.45	-0.23	0.19	-0.57	0.63	-0.19	0.04
DHK-Sal	0.36	0.29	0.22	1.45	1.54	0.96	0.96	0.83
Acquisition of Conditioned Threat – Mean Normalized Vigilant Head Turns to CS								
Saline	3.33	2.33	0.33	8.17	5.17	-	5.33	4.11
Mus-Bac	1.33	-0.17	-1.67	-0.67	0.83	-	0.17	-0.03
DHK	1.83	0.33	1.17	4.17	2.83	-	-2.17	1.36
MB-Sal	-2.00	-2.50	-2.00	-8.83	-4.33	-	-5.17	-4.14
DHK-Sal	-1.50	-2.00	0.83	-4.00	-2.33	-	-7.50	-2.75
Acquisition of Conditioned Threat – Blood pressure rise to snake (US - CS)								
MB-Sal	2.92	-1.85	9.60	12.08	3.10	-3.73	5.50	3.69
DHK-Sal	-3.45	6.57	3.56	-5.89	0.54	3.37	3.90	0.78
Appetitive Discriminative Conditioning – (CS+ - CS-) Appetitive Head Jerks								
Saline	14	11	19	3	18	9	6	11.43
Mus-Bac	20	15	24	16	17	14	10	16.57
DHK	9	6	9	5	12	8	3	7.43
MB-Sal	6	4	5	13	-1	5	4	5.14
DHK-Sal	-5	-5	-10	2	-6	-1	-3	-4.00

Table S1. Individual data points across the rostrocaudal axis of area 14 cannulated animals. Total number of infusions in each animal are indicated in the first row. Data is then presented for the human intruder test (as EFA scores), acquisition of conditioned threat (as the mean number of vigilant head turns for all the snake-associated CS presentations), blood pressure rise to the snake during acquisition of conditioned threat (US – CS) and appetitive Pavlovian discrimination (as the CS+ minus CS- difference in appetitive head jerks). IA Dist. row indicates the distance in millimeters from the interaural line. Symbols used to denote subject are consistent with those used across the paper. Data in bold shows the specific effects of each treatment, by subtracting the values obtained with drug treatment from the saline control (Mus-Bac = MB). Rows highlighted in gray indicate drug treatments which were found to be significant. Overall, there was no obvious difference in the effects of the manipulation in individual animals related to the rostro-caudal extent of their cannulae locations. While there appeared to be a trend for higher EFA scores in DHK-infused animals with more caudal cannulae placements, one of the three animals whose cannulae were more rostrally positioned had a high EFA score at saline (hexagonal symbol) and so was already close to ceiling. Likewise, larger overall reductions in conditioned acquisition responses in MB-infused animals with more caudal placements were somewhat confounded by higher overall levels after saline infusions.