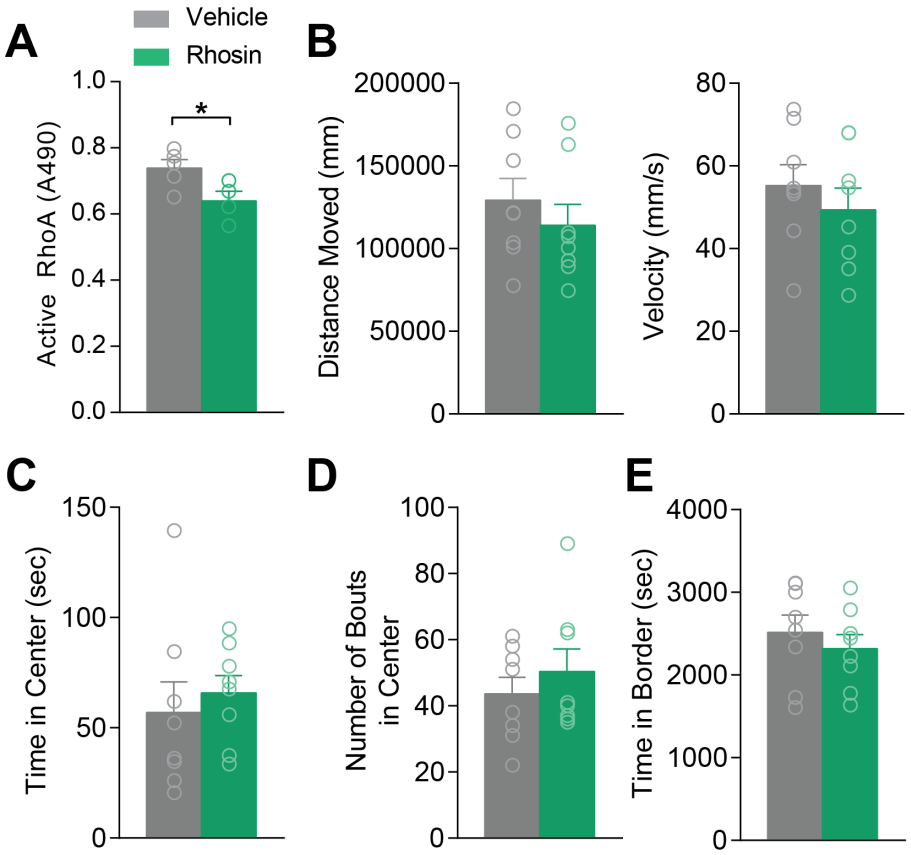
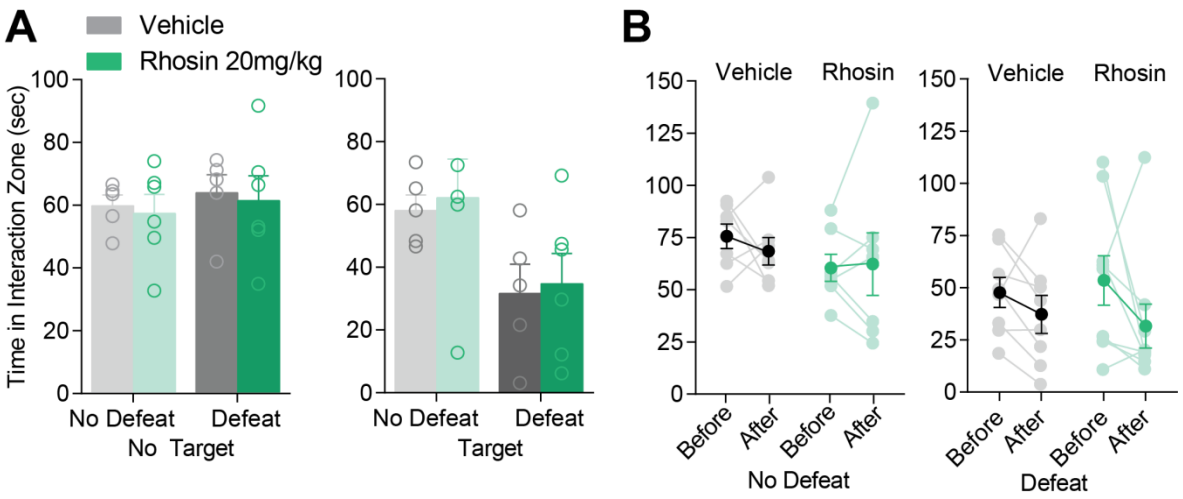
The Selective RhoA Inhibitor Rhosin Promotes Stress Resiliency Through Enhancing D1-Medium Spiny Neuron Plasticity and Reducing Hyperexcitability

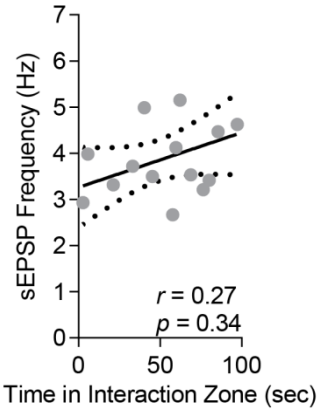
Supplemental Information



Supplemental Figure S1. Rhosin inhibits RhoA *in vivo* and does not alter baseline behaviors. (A) Rhosin decreases the amount of active RhoA following a single defeat session (two-tailed t_7=2.53, p=0.04, n=5,4 mice per group). **(B)** Distance traveled (two-tailed t_{14}=0.83, p=0.42, n=8 mice per group) and velocity (two-tailed t_{14}=0.81, p=0.43, n=8 mice per group) in an open field was not affected by Rhosin administration. **(C)** Time in the center of an open field was not affected by Rhosin administration (two-tailed t_{14}=0.55, p=0.59, n=8 mice per group). **(D)** The number of entries in to the center was not different among treatment groups (two-tailed t_{14}=0.80, p=0.44, n=8 mice per group). **(E)** The time mice spent in the border did not vary across treatment (two-tailed t_{14}=0.74, p=0.47, n=8 mice per group).



Supplemental Figure S2. Low doses of Rhosin or Rhosin administration after defeat does not restore defeat-induced social aversion. (A) Mice displayed no difference in interaction zone time in the no target condition (Two-way ANOVA no interaction $F_{1,18}$=0.51, P=0.999). Defeat mice displayed avoidance regardless of treatment (Two-way ANOVA no interaction $F_{1,18}$=0.002, P=0.96; main effect of defeat $F_{1,18}$=0.51 P=0.01). For this experiment N=5-6 mice per group. **(B)** 7 days of Rhosin (40mg/kg) administration after defeat does not alter stress-induced social aversion (Defeat: Two-way repeated measures ANOVA no interaction $F_{1,15}$=0.449, P=0.51; No defeat: Two-way repeated measures ANOVA no interaction $F_{1,12}$=0.449, P=0.52).



Supplemental Figure S3. No correlation is observed between sEPSP frequency and behavior.

Supplemental Table S1. Table of Statistics

Figure	Panel	Test	Subcategory	Test Statistic	Exact *P*-value
1	B	Two-way ANOVA	No Target	No Interaction $F_{1,73}$=0.66	0.4188
			Target	Interaction $F_{1,73}$=4.50 Main effect of defeat $F_{1,73}$=28.05	0.0373 <0.0001
	C	Two-way ANOVA	Distance	No Interaction $F_{1,55}$=0.79	0.3781
			Velocity	No Interaction $F_{1,55}$=0.45	0.5037
	D	Two-way ANOVA		Interaction $F_{1,33}$=4.24	0.0474
2	B	Two-way ANOVA		No Interaction $F_{1,14}$=0.51	0.4872
	D	Two-way ANOVA		Interaction $F_{1,14}$=7.43	0.0184
3	A	Two-way ANOVA repeated measures		Interaction $F_{18,254}$=3.93	<0.0001
	B	Two-way ANOVA		Interaction $F_{1,62}$=7.59	0.0077
	C	Pearson Correlation		r=0.40	0.0312
	D	Two-way ANOVA		Interaction $F_{1,62}$=4.23	0.0438
	E	Two-way ANOVA repeated measures		No Interaction $F_{24,456}$=3.388 Main effect of defeat $F_{1,59}$=3.311 No defeat Rhosin vs. Defeat Vehicle	<0.0001 0.0263 <0.05
	F	Two-way ANOVA		No Interaction $F_{1,59}$=0.03 Main effect of defeat $F_{1,59}$=15.87	0.8574 0.0002
4	B	Two-way ANOVA		No Interaction $F_{1,28}$=1.15 Main effect of defeat $F_{1,28}$=14.73	0.2932 0.0006
	C	Two-way ANOVA		No Interaction $F_{1,28}$=2.31 Main effect of defeat $F_{1,28}$=14.20	0.1395 0.0008
	D	Two-way ANOVA		No Interaction $F_{1,28}$=0.16 Main effect of defeat $F_{1,28}$=13.50	0.6920 0.0010
	E	Two-way ANOVA		No Interaction $F_{1,23}$=0.23	0.6348
5	C	Kolmogorov–Smirnov test		Defeat Rhosin vs Defeat Vehicle D=0.19	<0.0001
	D	Two-way ANOVA	Frequency	Interaction $F_{1,51}$=4.85	0.0325
			Amplitude	Interaction $F_{1,51}$=5.78	0.0200
6	B	Two-way ANOVA		Interaction $F_{1,32}$=5.31	0.0279
	C	Two-way ANOVA	Thin	Interaction $F_{1,32}$=7.03	0.0124
			Stubby	Interaction $F_{1,32}$=0.18	0.6781
			Mushroom	Interaction $F_{1,32}$=6.62	0.0151
	D	Pearson Correlation		r=0.48	0.0122