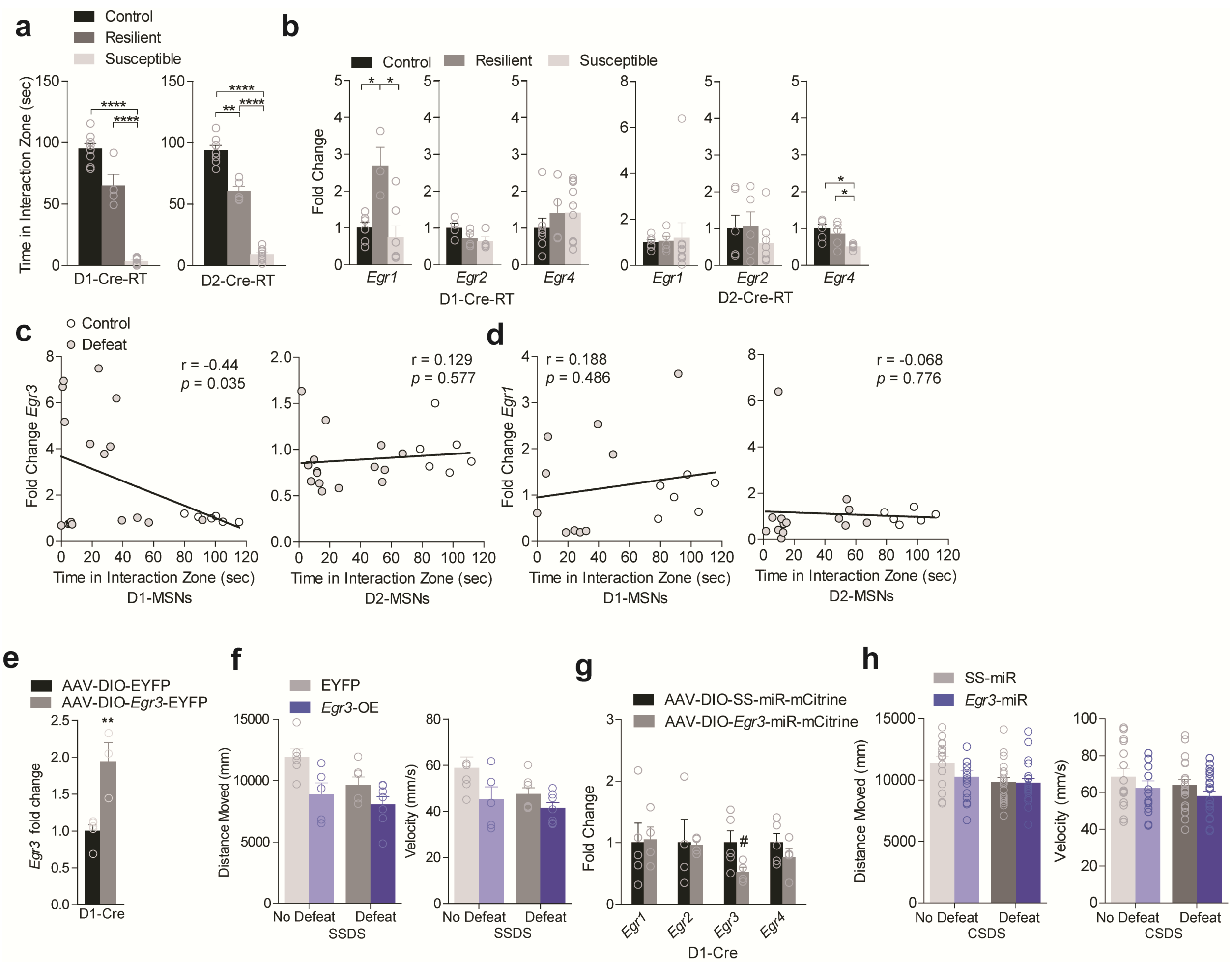
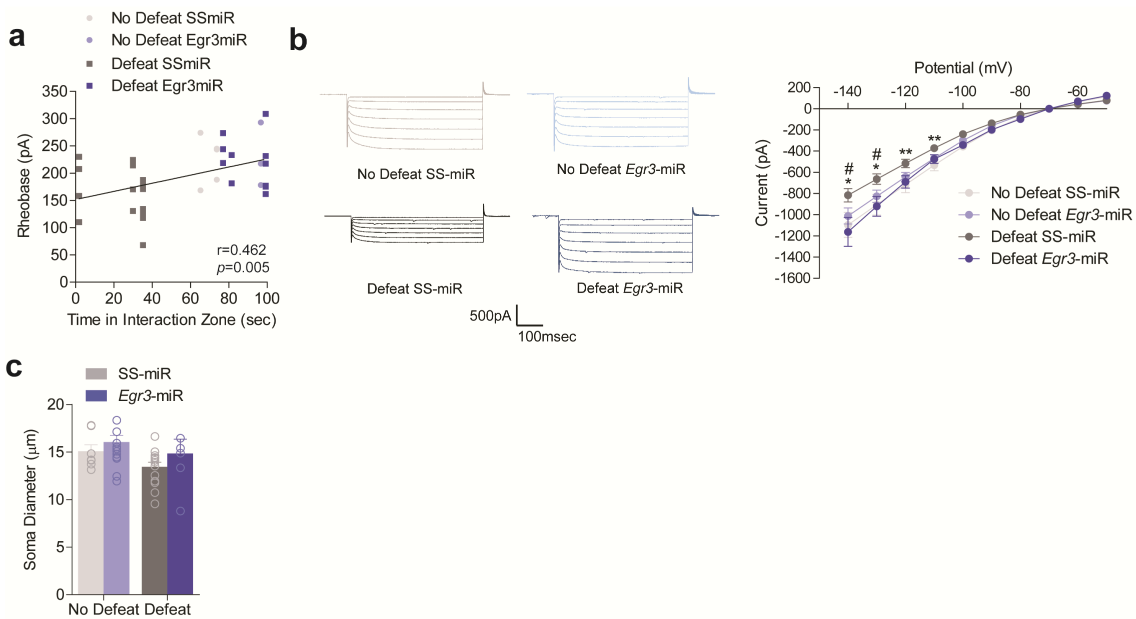
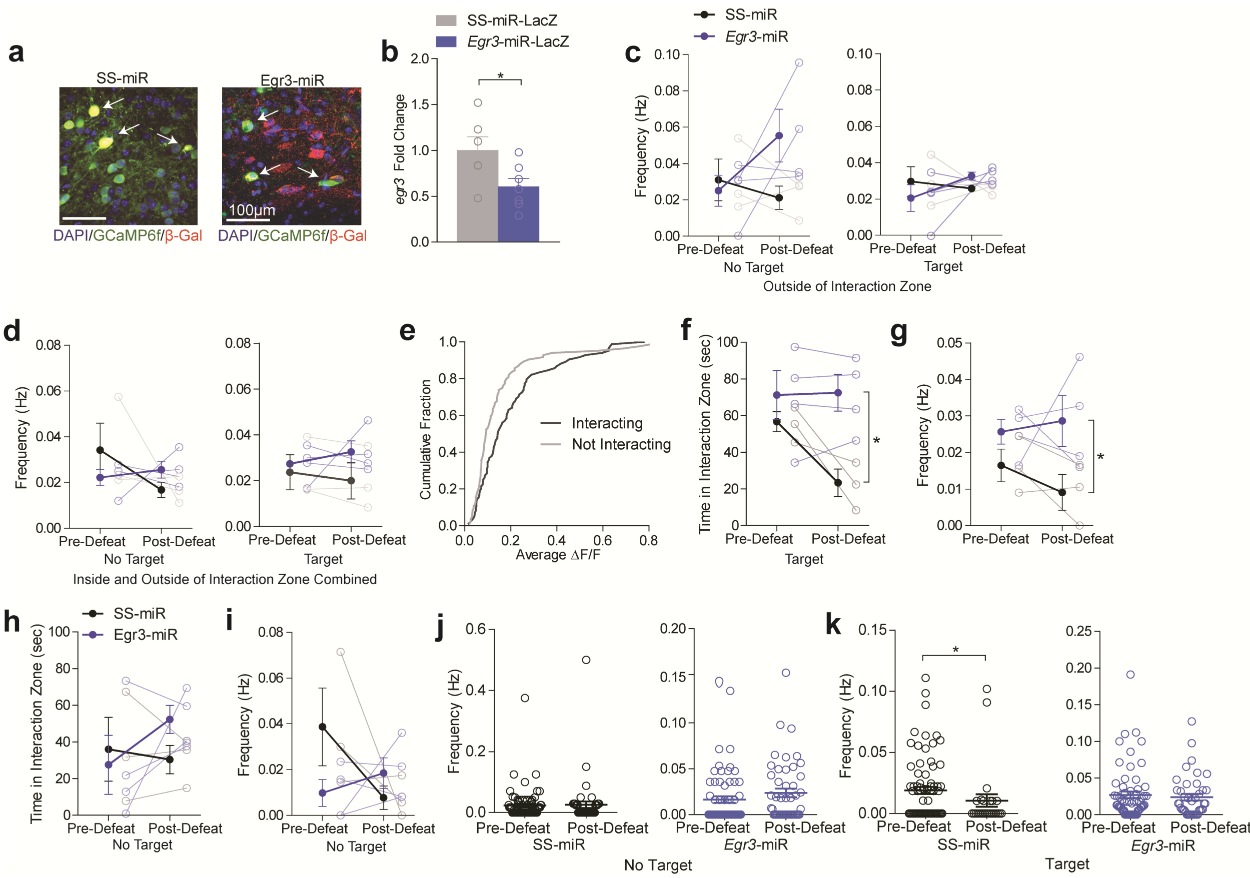


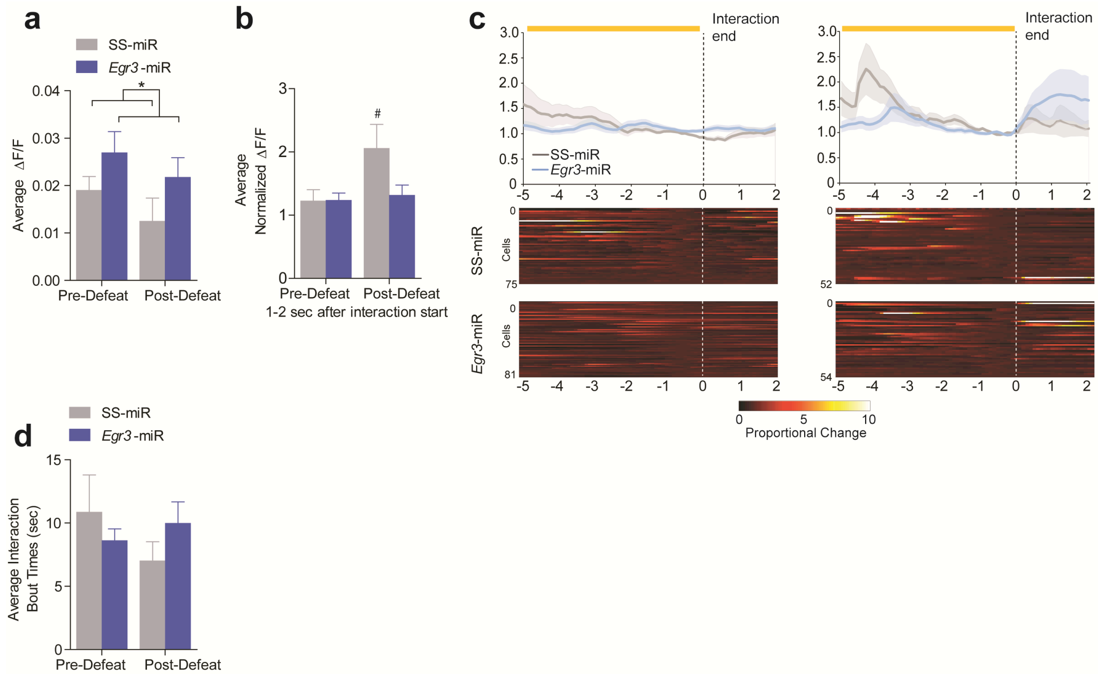
Supplementary Figure 1. D1-Cre-RiboTag (RT) and D2-Cre-RT behavior, *Egr* expression, and locomotor measures. (**a**) Defeat significantly reduced time in the interaction zone in both RT animal lines (D1-Cre-RT, $F_{2,19}$=134.4, p<0.0001, n=4-8 pooled mice per group; D2-Cre-RT, $F_{2,19}$=187.5, p<0.0001, n=4-8 pooled mice per group). (**b**) Egr expression in MSN subtypes. D1-Cre-RT: *Egr1* is up-regulated in resilient mice ($F_{2,16}$=8.61, p<0.01), while no change is observed in *Egr2* ($F_{2,11}$=2.35, p>0.05) or *Egr4* ($F_{2,20}$=0.66, p>0.05; n=4-10 samples per group for each gene analyzed). D2-Cre-RT: *Egr4* is downregulated in susceptible mice ($F_{2,19}$=9.68, p<0.01) with no change in *Egr1* ($F_{2,20}$=0.50, p>0.05) or *Egr2* ($F_{2,18}$=0.68, p>0.05). (**c**) A significant negative correlation between *Egr3* expression and time in the interaction zone was observed in D1-MSNs only. (**d**) No correlation was observed between *Egr1* expression and time in the interaction zone in both subtypes. (**e**) *Egr3*-OE significantly enhanced *Egr3* expression in the NAc of D1-Cre mice (t_6=4.27, p<0.01). (**f**) No difference was observed in distance moved ($F_{1,20}$=1.03, p>0.05, n=5-7 mice per group) or velocity ($F_{1,20}$=0.97, p>0.05, n=5-7 mice per group) following D1-MSN Egr3-OE in defeated and non-defeated conditions. (**g**) *Egr3*-miR reduced *Egr3* expression in the NAc of D1-Cre mice (t_7=2.06, p=0.0783), but not other Egr genes. (**h**) No difference was observed in distance moved ($F_{1,26}$=0.06, p>0.05, n=6-9 mice per group) or velocity ($F_{1,26}$=0.09, p>0.05, n=6-9 mice per group) following D1-MSN Egr3-miR expression in defeated and non-defeated conditions.



Supplementary Figure 2. Rectification in NAc D1-MSNs is attenuated in defeat mice. (**a**) A significant positive correlation was observed between rheobase and time in the interaction zone. (**b**) Defeated mice injected with SS-miR displayed reduced rectification as demonstrated by smaller current plateaus produced by negative voltage deflections ($F_{21,245}$=2.17, p<0.01, N(n)= 3-4(7-14)). Capacitive transients are removed for clarity. No defeat SS-miR vs. defeat SS-miR; *p<0.05, **p<0.01; #p<0.05 defeat SS-miR vs. defeat *Egr3*-miR. (**c**) Soma diameter remained unaltered across groups ($F_{1,38}$=0.06, p>0.05; 6-15 cells per group).



Supplementary Figure 3. GCaMP6f expression and behavior dependent frequency alterations. (**a**) Expression of LacZ reporter with AAV2.2-DIO-Egr3miR-LacZ is colocalized with GCaMP6f D1-MSN expressing cells. Arrows indicate examples of colocalization of LacZ and GCaMP6. Arrows indicate overlap. (**b**) Egr3 is significantly knocked down in the NAc of D1-Cre mice injected with AAV2.2-DIO-Egr3-miR-LacZ in comparison to AAV2.2-DIO-SS-miR-LacZ controls (t_{11}=2.36, p<0.05, n=4-9 samples per group). (**c**) No difference was observed in social interaction in the no target condition ($F_{1,5}$=1.84 p>0.05). (**d**) No differences were observed in frequency when mice were outside of the interaction zone in the no target ($F_{1,5}$=2.97, p>0.05) and target ($F_{1,5}$=1.41, p>0.05) conditions. (**e**) A rightward shift in the distribution of ΔF/F events is observed when animals are within the interaction zone (IZ) versus outside of the interaction zone (IZ) (Kolmogorov-Smirnov test D=0.23, p<0.01). (**f-g**) Means represented with individual animals for time in the interaction zone and frequency measures, respectively. (**h**) No difference was found in frequency of calcium transients when times were averaged across the entire social interaction session in the no target and target condition (no target $F_{1,5}$=1.94, p>0.05; target $F_{1,5}$=0.77, p>0.05). (**i**) Frequency of calcium events is unchanged following defeat in the no target condition ($F_{1,5}$=4.74, p>0.05, n=3-4 cells per group). (**j**) No differences were observed in individual cell firing frequency in the no target condition (SS-miR Mann-Whitney U(4943, 2932) p>0.05; *Egr3*-miR Mann-Whitney U(3508, 3047) p>0.05). (**k**) Individual cell firing frequency was significantly reduced in SS-miR mice after defeat (Mann-Whitney U(6590, 2863) p<0.001), but not in *Egr3*-miR mice (Mann-Whitney U(3353, 2107) p>0.05).



Supplementary Figure 4. Magnitude of calcium transients differs among SS-miR and *Egr3*-miR mice. (**a**) The average ΔF/F amplitude was significantly enhanced by *Egr3* knockdown (Main effect of virus $F_{1,208}$, $p<0.05$). (**b**) The magnitude of normalized ΔF/F amplitude is increased in SS-miR mice by defeat (Interaction $F_{1,19301}=4.57$, $p<0.0001$; Main effect of knockdown $F_{1,19301}=6.02$, $p<0.05$). (**c**) Average normalized ΔF/F traces showing calcium activity 5sec prior to and 2sec following the termination of a social interaction bout. Calcium transient magnitude is increased above baseline before the end of social interaction after defeat in SS-miR mice (See **Supplementary Table 3**). (**d**) Average individual bout times of SS-miR mice compared to *Egr3*-miR mice.

Supplemental Movie 1. Processed calcium signal and behavior of a SS-miR mouse following defeat. *Left* Example of a registered and background subtracted video used for analysis. *Right* SS-miR mouse in the social interaction test following defeat.

Supplemental Movie 2. Processed calcium signal and behavior of an Egr3-miR mouse following defeat. *Left* Example of a registered and background subtracted video used for analysis. *Right* Egr3-miR mouse in the social interaction test following defeat.

Supplementary Table 1. Primer list for qPCR and ChIP

	Gene	Direction	Sequence
qPCR	*Gapdh*	forward	AGGTCGGTGTGAACGGATTTG
		reverse	TGTAGACCATGTAGTTGAGGTCA
	Egr1	forward	CTCCCTTCAGCGCTAGACC
		reverse	ATGCTGTACAAAGATGCAGGG
	Egr2	forward	GAAGGAACGGAAGAGCAGTG
		reverse	AGCCAGAGCTTCATCTCACG
	Egr3	forward	ACTCGGTAGCCCATTACAATC
		reverse	TGGCTGGAAAGAGCTCGAAT
	Egr4	forward	ACCCACAGAACAGGCACTTC
		reverse	ACTTCCCCAGCTTGTCTCTG
ChIP	*RhoA*	forward	CAGGGCGTGGATGCGT
		reverse	GACGTGCGCGGCCCCGAG
	RhoB	forward	GCGCATCCAAGCCTATGAC
		reverse	CAGCCATTCTGGGATCCGTA
	RhoC	forward	TCCCCAAAGCTTCCTCAACC
		reverse	GCATGGAGTCCTACAAGGATG
	Cdc42	forward	CGCCCAGGAGTTACTTTTCG
		reverse	TGAAGGTGAAGGTGGGAAGG
	Kalrn	forward	TGGTTGAGCATCTGGCTTCT
		reverse	GGAGAAGGCCACGGTTAAAA
	Rhobtb2	forward	CCAGGAGTCTGGGTCTCCA
		reverse	GTGAGATGTCTGGGGTCACT
	Shank2	forward	GGGAGAGACACAGAGCTGG
		reverse	GGAATGTAGTGTGCAGCAGG
	Actn1	forward	GAGCACAGTGCCATTTGGT
		reverse	TGTGCATATAGGTGGACTGGG
	Arc	forward	TTCTCTGCTTGTTTCCCCTCC
		reverse	TGAGAGGAATGTCTTTCTGGG
	Mmp25	forward	TTTCGGTCTCCCGTTGCT
		reverse	CTGTGTGATCCCAGTTGCG
	Rap1a	forward	TAAATAGATTCCGGACACAGCG
		reverse	AGAGGAGGGAGGAGGAGGA
	GSK3a	forward	CTTCTACCCCCTCAGCTCTC
		reverse	AAGGAGAAGTGGGAACCTCC
	CREB	forward	CCGG GAAGTAGCCGAAGG
		reverse	GCCACTCACGGAAACAGC
	CamKIIa	forward	CGTCCCCACAGCATCTTCT
		reverse	CCTTGCTCCTCTTGTCCCC

Supplementary Table 2. Table of Statistics

Figure	Panel	Test	Panel	Test Statistic	Exact P-value
1	b	One-way ANOVA	D1-MSN	$F_{2,22}$=4.98	0.0176
		One-way ANOVA	D2-MSN	$F_{2,20}$=0.51	0.6088
	d	Two-way ANOVA	No Target	interaction: $F_{1,30}$=2.79	0.1053
		Two-way ANOVA	Target	interaction: $F_{1,30}$=7.01	0.0128
				main effect virus: $F_{1,30}$=10.41	0.0030
				main effect defeat: $F_{1,30}$=39.11	<0.0001
	e	Two-way ANOVA	No Target	interaction: $F_{1,71}$=3.13	0.0811
		Two-way ANOVA	Target	interaction: $F_{1,71}$=11.88	0.0010
				main effect virus: $F_{1,71}$=6.22	0.0150
				main effect defeat: $F_{1,71}$=37.34	< 0.0001
	f	Two-way ANOVA	Sucrose Pref	interaction: $F_{1,36}$=4.26	0.0462
2	a	Kolmogorov–Smirnov test	Cumulative Probility Plot	No defeat SS-miR vs. Defeat SS-miR D_{2973}=0.12	< 0.0001
		Two-way ANOVA	Frequency	interaction: $F_{1,55}$=6.54	0.0340
				main effect virus: $F_{1,55}$=6.54	0.0134
				main effect defeat: $F_{1,55}$=4.19	0.0456
		Two-way ANOVA	Amplitude	interaction: $F_{1,55}$=2.78	0.1010
	b	Two-way ANOVA		interaction: $F_{1,33}$=22.46	<0.0001
				main effect virus: $F_{1,33}$=18.57	0.0001
	c	Two-way ANOVA	Thin	interaction: $F_{1,33}$=8.71	0.0058
				main effect virus: $F_{1,33}$=7.53	0.0097
				main effect defeat: $F_{1,33}$=4.42	0.0432
			Stubby	interaction: $F_{1,33}$=12.43	0.0013
				main effect virus: $F_{1,33}$=15.00	0.0005
				main effect defeat: $F_{1,33}$=4.86	0.0346
			Mushroom	interaction: $F_{1,33}$=3.44	0.0724
3	a	Two-way RM ANOVA	Rheobase	interaction: $F_{1,42}$=7.25	0.0102
			I vs. APs	interaction: $F_{15,240}$=2.06	0.0127
				main effect current: $F_{15,240}$=174.3	< 0.0001
	b	Two-way ANOVA		interaction: $F_{1,58}$=10.46	0.0020

	c	Two-way ANOVA		interaction: $F_{1,52}$=4.37	0.0415
				main effect virus: $F_{1,52}$=7.76	0.0075
				main effect defeat: $F_{1,52}$=4.55	0.0377
	d	Two-way RM ANOVA	Sholl Analysis	interaction: $F_{33,308}$=2.10	0.0006
				main effect distance: $F_{33,308}$=122.4	$<$ 0.0001
	e	Two-way ANOVA		interaction: $F_{1,28}$=9.31	0.0049
	f	Two-way ANOVA		interaction: $F_{1,28}$=6.74	0.0148
				main effect of virus: $F_{1,28}$=11.25	0.0023
4	a	t-test	no target	t_{13}=1.21	0.2474
			target	t_{13}=5.24	0.0002
	b	t-test	*RhoA*	t_{12}=2.35	0.0364
			RhoB	t_{13}=2.15	0.0506
			RhoC	t_{13}=0.55	0.5951
			Cdc42	t_{13}=0.07	0.9472
			Kalrn	t_{13}=0.09	0.9333
			Rhobtb2	t_{12}=0.01	0.9923
			Shank2	t_{12}=2.79	0.0164
			Actn1	t_{12}=2.49	0.0286
			Arc	t_{13}=0.05	0.9583
			Mmp25	t_{13}=0.52	0.6126
			Rap1a	t_{13}=0.35	0.7318
			GSK3a	t_{13}=0.12	0.9058
			CREB	t_{13}=1.25	0.2324
			CamKIIa	t_{12}=2.29	0.0507
5	c	Two-way RM ANOVA		interaction: $F_{1,5}$=10.82	0.0217
				main effect of defeat time: $F_{1,5}$=9.31	0.0284
	d	Two-way RM ANOVA		interaction: $F_{1,5}$=7.98	0.0085
				main effect virus: $F_{1,5}$=6.33	0.0167
				main effect defeat time: $F_{1,5}$=8.76	0.0143
	e	See **Supplementary Table 3-4**			