Science Advances
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Supplementary Materials for

Targeted epigenomic editing ameliorates adult anxiety and excessive drinking after adolescent alcohol exposure

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Published 4 May 2022, *Sci. Adv.* **8**, eabn2748 (2022)
DOI: 10.1126/sciadv.abn2748

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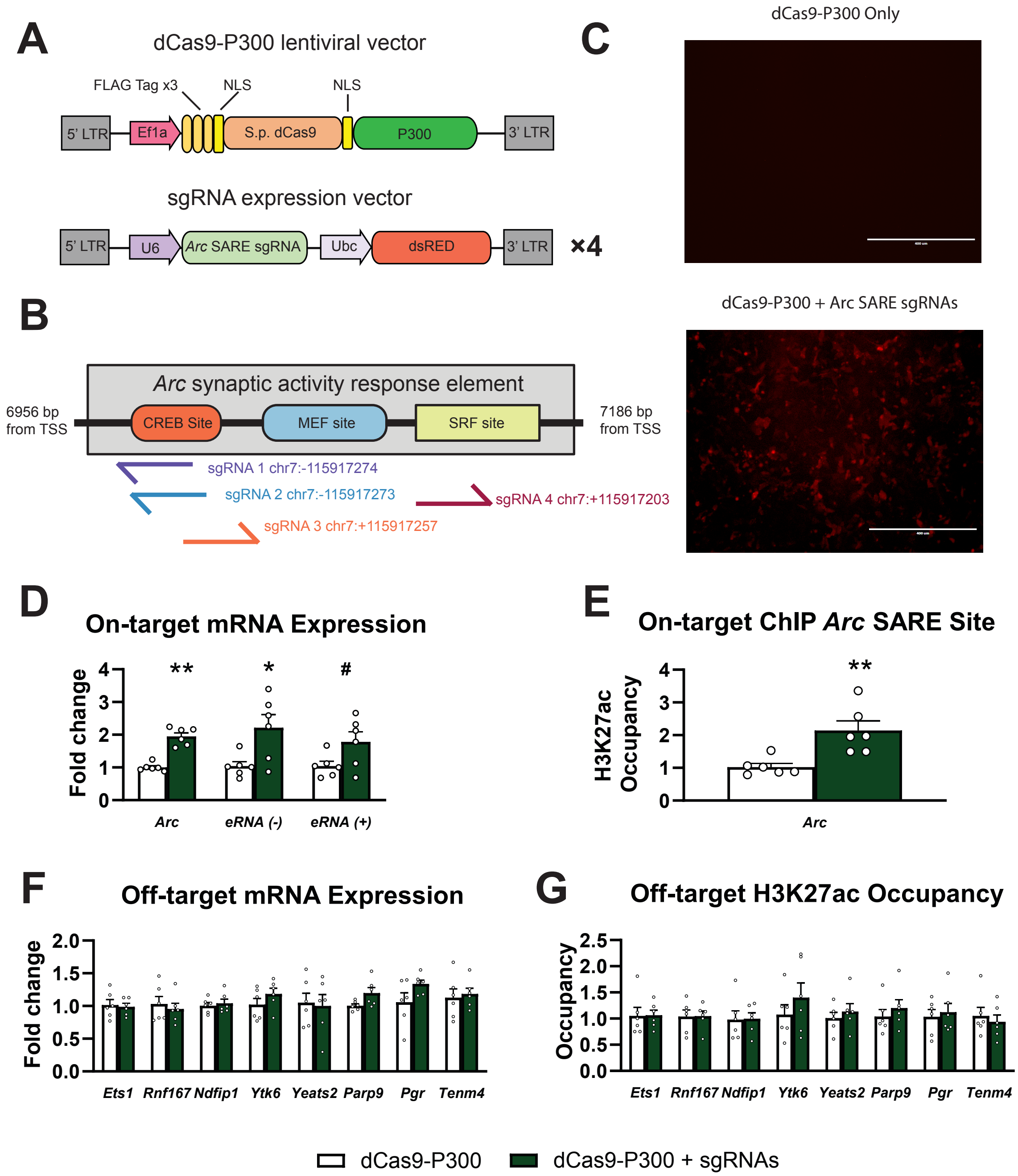

Fig. S1. Design of dCas9-P300 vector and sgRNAs for the *Arc* SARE site as well as *in vitro* experiments in PC12 cells. A) Diagram of dCas9-P300 vector and sgRNAs for *Arc* SARE. B) Diagram of the SARE site of the *Arc* gene and locations of four guided RNAs (sgRNAs) that were developed and used in the study. C) PC12 cells were treated with either dCas9-P300 only or dCas9-P300 plus SARE sgRNAs tagged with mCherry (Ds-Red protein) and these images (scale bar, 400 μm) show transductions in cells treated with dCas9-P300 + SARE sgRNAs. D) Bar diagram showing that epigenomic editing at SARE site with dCas9-P300 in PC12 cells significantly increased *Arc* mRNA

(Mann-Whitney test, U=36, p=0.002) and (-) eRNA (t_{10}=2.808, p=0.019) levels as well as (E) increases (t_{10}=3.580, p=0.005) in occupancy of H3K27ac at *Arc* SARE site after transduction with dCas9-P300 + sgRNAs. F) dCas9-P300 + sgRNAs transduction did not change mRNA levels of off-target genes. G) Transduction of dCas9-P300 + sgRNAs did not increase occupancy of H3K27ac at predicted off-target genomic locations. Bar graphs show mean ± SEM (n=6) and individual values are shown with circle dots on bar graphs. *p<0.05, **p<0.01 are significantly different from control groups (dCas9-P300 only). # (+) eRNA (t_{10}=2.184, p=0.0.054).

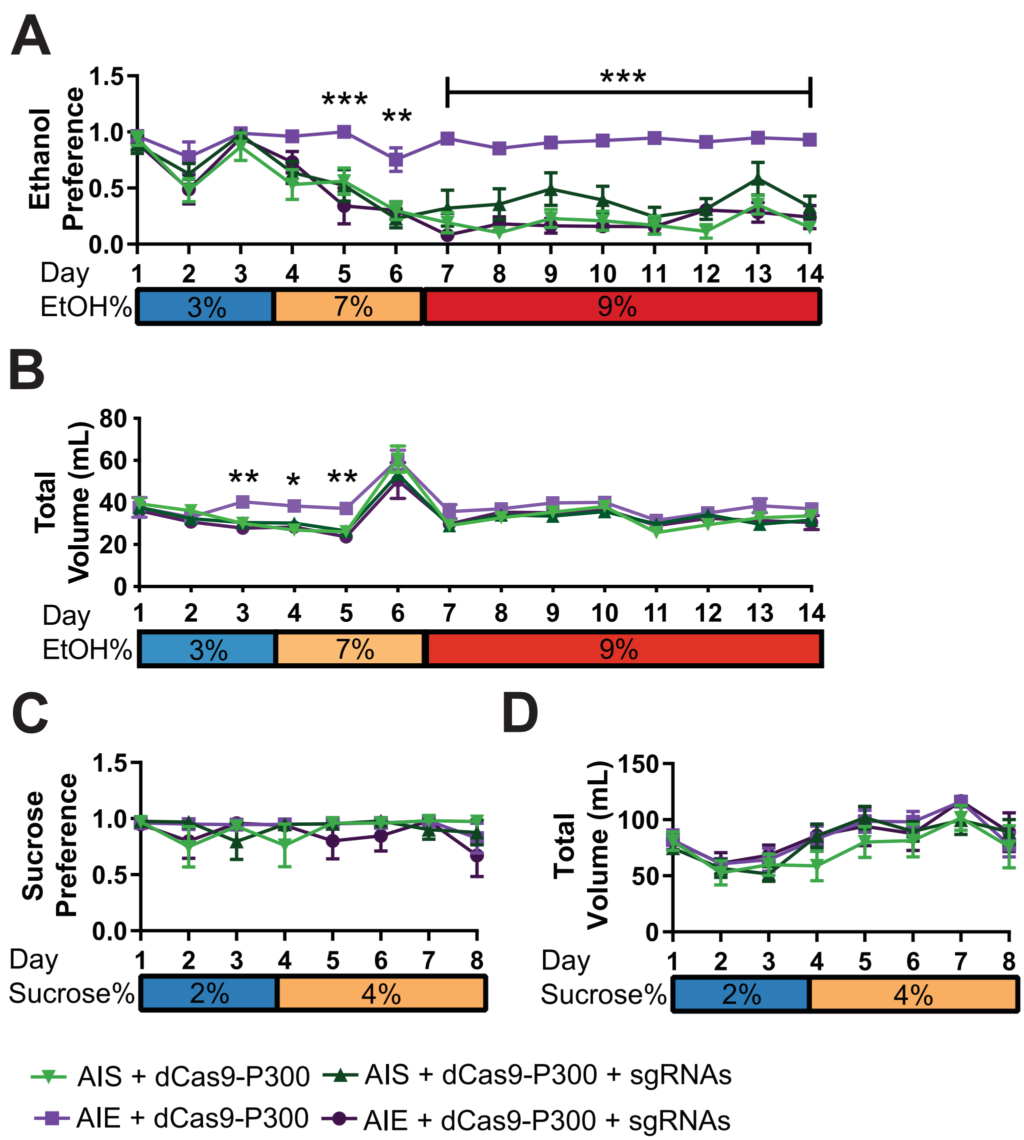

Fig. S2. Effects of the infusion of dCas9-P300 or dCas9-P300 plus *Arc* SARE sgRNAs into central nucleus of amygdala (CeA) on alcohol and sucrose drinking measures in AIS and AIE adult rats. A) AIE exposure significantly increased alcohol preference which is attenuated by the infusion of dCas9-P300 plus sgRNAs of *Arc* SARE into CeA (lentivirus x day interaction, $F_{39,247}$=2.932, p<0.001). Other groups show no changes in alcohol preference. B) dCas9-P300 + sgRNAs infusion into CeA have no effects on total fluid intake (mL/day) either in AIS or AIE adult rats at the higher doses of ethanol intake. C) dCas9-P300 + sgRNAs infusion into CeA have no effects on sucrose preference or total fluid intake (D) in AIS and AIE adult rats. Each value represents mean ± SEM (n=5-6 rats) for each day either for alcohol or sucrose intake. *p<0.05, **p<0.01, and ***p<0.001 are significantly different from respective control groups (AIE rats infused with dCas9-P300 vs AIE rats infused with dCas9-P300+ sgRNAs).

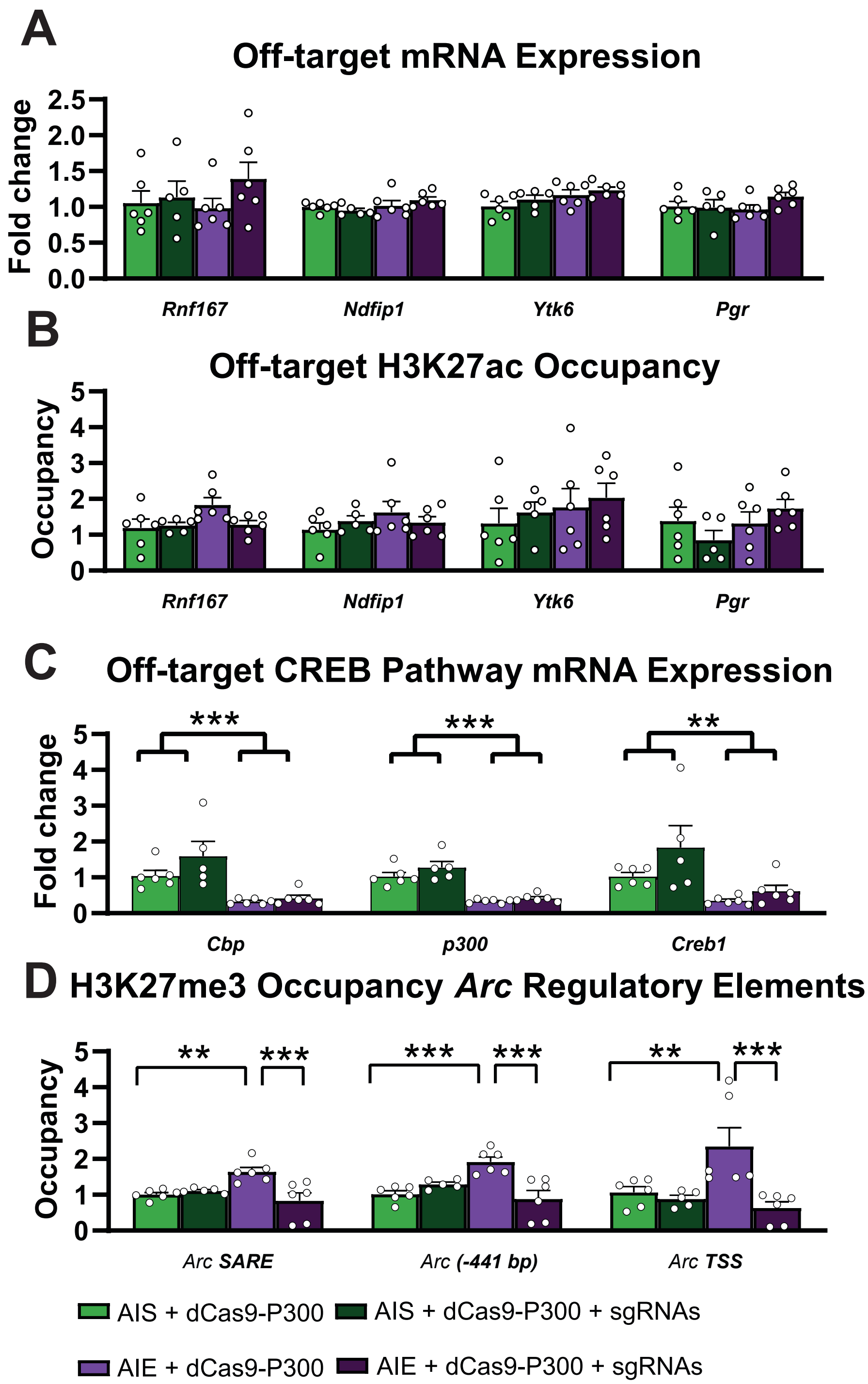

Fig. S3 Effects of in vivo CeA-infusion of dCas9-P300 or dCas9-P300 plus sgRNAs on off-target gene expression and histone acetylation (H3K27ac) as well as histone methylation (H3K27me3) of *Arc* regulatory sites in the amygdala of AIS and AIE adult rats. Infusion of dCas9-P300 plus sgRNAs of *Arc* SARE into CeA has no effects on the expression (A) and occupancy of H3K27ac (B) of off-target genes in the amygdala of AIS and AIE adult rats. C) Bar diagram showing that AIE significantly decreased the expression of various genes of the CREB pathway (*Cbp*, adolescent exposure, $F_{1,19}$= 23.196, p<0.001; *p300*, adolescent exposure $F_{1,19}$= 64.551, p<0.001 and *Creb1*, adolescent exposure, $F_{1,19}$= 11.426, p=0.003) in adult amygdala, which are not modulated by the infusion of dCas9-P300 + sgRNAs into the CeA of AIE adult rats. D) AIE significantly increased the occupancy of H3K27me3 at *Arc* regulatory sites (*Arc* SARE, adolescent exposure x lentivirus infusion, $F_{1,19}$= 11.327, p=0.003, *Arc* -441bp, adolescent exposure x lentivirus infusion, $F_{1,19}$= 18.30, p<0.001, and *Arc* TSS, adolescent exposure x lentivirus infusion, $F_{1,19}$= 6.541, p=0.019), which was normalized by the infusion of dCas9-P300 + sgRNAs into CeA of AIE adult rats. Bar graphs show mean ± SEM (n=5-6) and individual values are shown with circle dots on bar graphs. Two-way ANOVA followed by Tukey test, **p<0.01, ***p<0.001 are significantly different from respective control groups (AIS+dCas9-P300 vs AIE rats infused with dCas9-P300 and AIE+ dCas9-P300 vs AIE rats infused with dCas9-P300 plus sgRNAs).

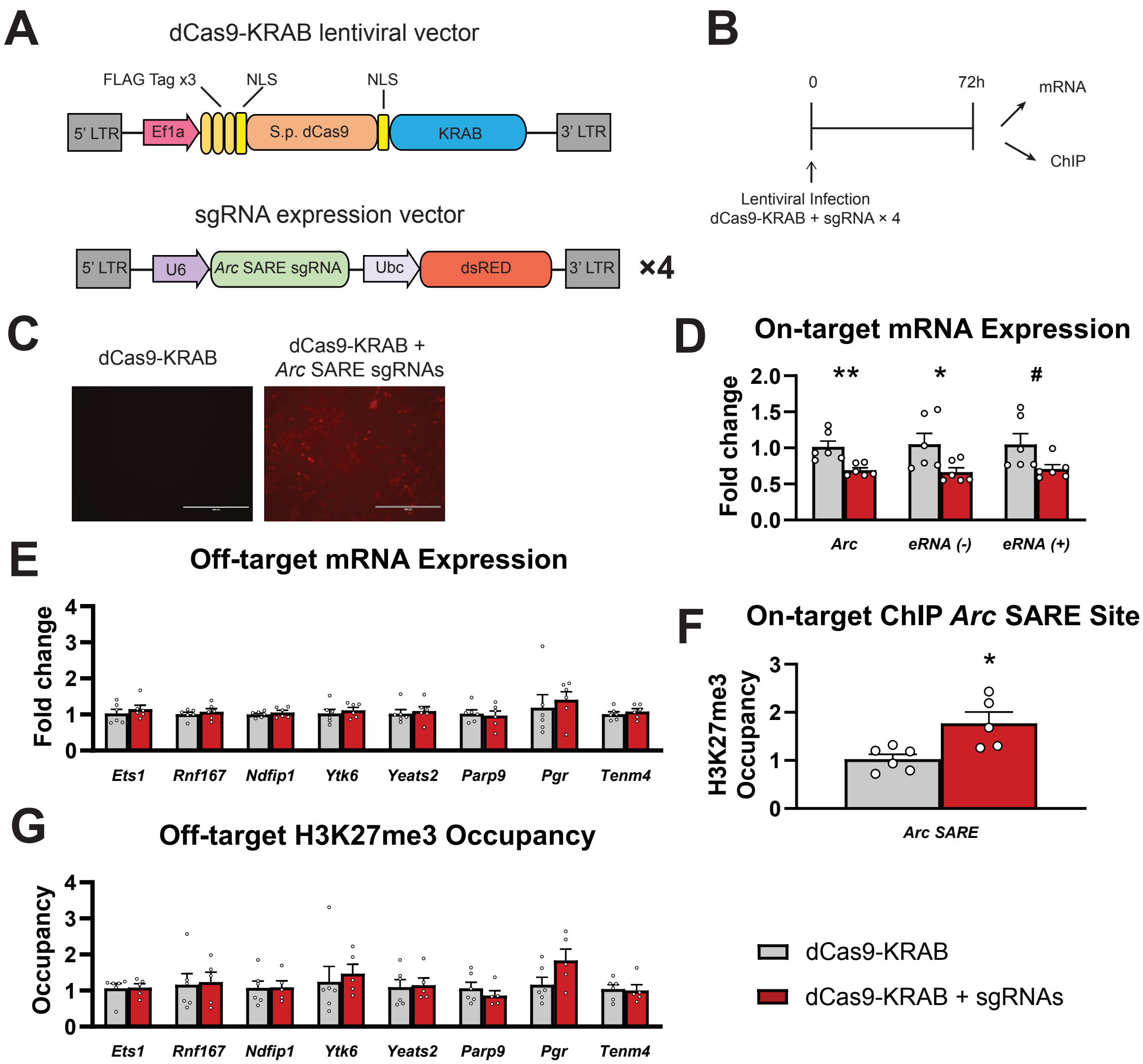

Fig.S4. Design of dCas9-KRAB vector and sgRNAs for the *Arc* SARE site as well as validation experiments in PC12 cells. A) This diagram represents the design of lentiviral vectors of dCas9-KRAB and sgRNAs for *Arc* SARE. B) PC-12 cells were treated with either dCas9-KRAB or dCas9-KRAB plus SARE sgRNAs (four sgRNAs together) tagged with mCherry (Ds-Red protein) and these images (scale bar, 400 µm) show transductions in cells (C) treated with dCas9-KRAB plus SARE sgRNAs. D) Bar diagram showing decreased *Arc* mRNA expression (t_{10}=3.684, p=0.004), (-) *Arc* eRNA (t_{10}=2.386, p=0.038), and (+) *Arc* eRNA (t_{10}=2.125, #p=0.059) levels after dCas9-KRAB plus sgRNAs treatment. E) dCas9-KRAB plus sgRNAs treatment did not change expression of predicted off-target genes, but increased H3K27me3 occupancy (Mann-Whitney test, U=2.0, p=0.017) at *Arc* SARE site (F). G) Treatment with dCas9-KRAB plus sgRNAs did not change H3K27me3 occupancy at predicted off-target genome sites. Values are mean ± SEM (n=5-6) and individual values are shown with circle dots on bar graphs. *p<0.05, **p<0.01 are significantly different from control groups (dCas9-KRAB only).

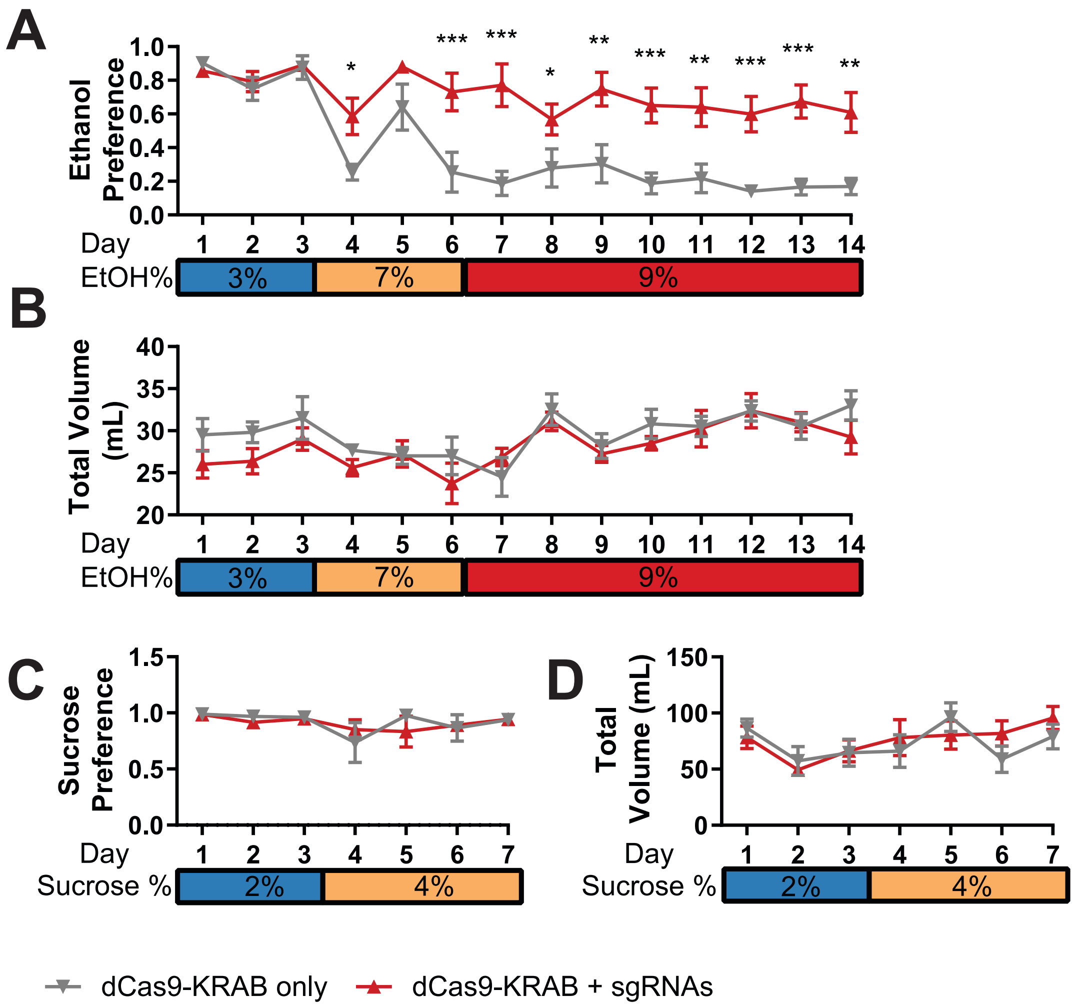

Fig. S5. Effects of in vivo CeA-infusion of dCas9-KRAB or dCas9-KRAB plus Arc SARE sgRNAs on alcohol and sucrose drinking measures in alcohol naïve control adult rats. A) Alcohol preference is significantly (lentivirus infusion x day interaction, $F_{13,156}$= 3.672, $p<0.001$) increased by the infusion of dCas9-KRAB plus sgRNAs of *Arc* SARE into CeA of control adult rats. B) dCas9-KRAB + sgRNAs infusion into CeA have no effects on total fluid intake (mL/day) in control rats. C) dCas9-KRAB + sgRNAs infusion into CeA have no effects on sucrose preference or total fluid intake (D) in control rats. Each value represents mean ± SEM for each day either for alcohol (n=6-8 rats) or sucrose (n=5-7 rats) intake. Two-way repeated measures ANOVA followed by Tukey test: *p<0.05, **p<0.01, and ***p<0.001 are significantly different from control groups (rats infused with dCas9-KRAB only into CeA).

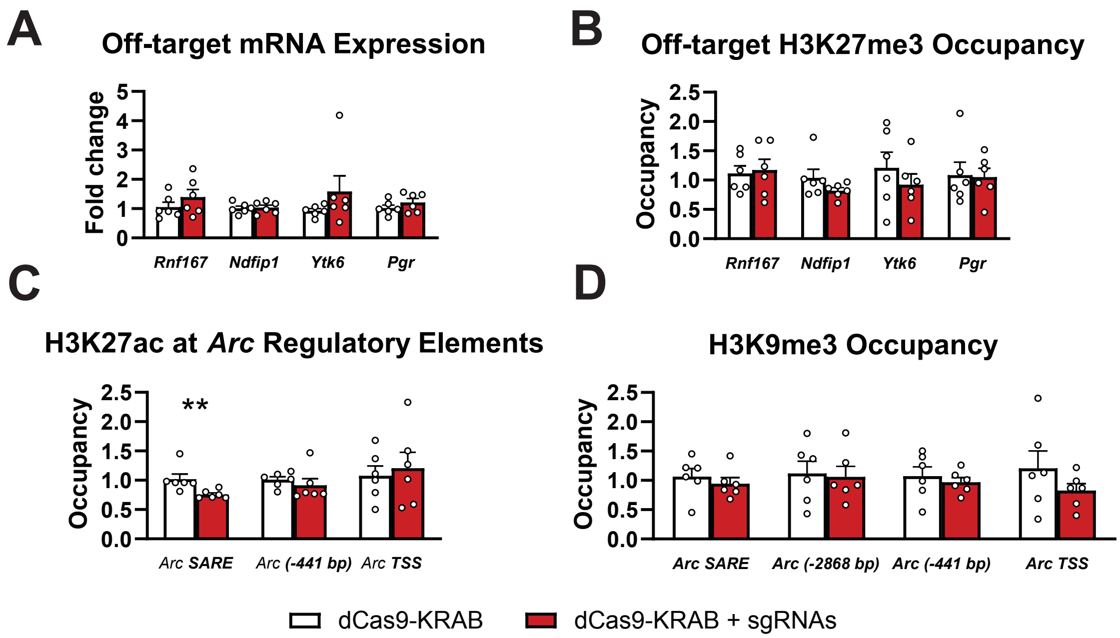

Fig. S6. Effects of in vivo CeA-infusion of dCas9-KRAB or dCas9-KRAB plus *Arc* SARE sgRNAs on off-target genes expression and histone trimethylation (H3K27me3) as well as histone acetylation (H3K27ac) and H3K9me3 of *Arc* regulatory sites in the amygdala of alcohol naïve control adult rats. A) Infusion of dCas9-KRAB plus sgRNAs into CeA has no effects on the expression and occupancy of H3K27me3 (B) of additional off-target genes in the amygdala of control rats. C) Bar diagram showing that dCas9-KRAB + sgRNAs infusion into CeA decreased the occupancy of H3K27ac at *Arc* SARE (Mann-Whitney rank sum test, U=1.0, p=0.004) but not at other sites of *Arc* gene in the amygdala. D) Bar diagram showing that dCas9-KRAB + sgRNAs infusion into CeA produced no change in occupancy of H3K9me3 at *Arc* SARE and other sites of *Arc* gene in the amygdala. Values are mean ± SEM (n=6 in each group) and individual values are shown with circle dots on bar graphs. **p<0.01 are significantly different from control groups (rats infused with dCas9-KRAB only into CeA).

Table S1: Various primers sequences used in qPCR, ChIP assay, and 3C-qPCR assay. Sequences for the single guide (sg) RNAs of *Arc* SARE site are also shown in the table.

Primer Name	Sequence (5' to 3')
RNA Primers	
Arc forward	ACA GAG GAT GAG ACT GAG GCA C
Arc reverse	TAT TCA GGC TGG GTC CTG TCA C
Creb1 forward	AGA AGC AGC ACG AAA GAG AG
Creb1 reverse	CAC TGC CAC TCT GTT CTC TAA A
Cbp forward	TAA TGG AGG CTG CCC AGT GTG TAA
Cbp reverse	CTG GCG GAG CTT GTG TTT GAT GTT
p300 forward	AAA CAC CAG CAA CGA GAG TAC CGA
p300 reverse	TCC ATG GTG GCG TAC AGT TTC TGA
Hprt1 forward	TCC TCA GAC CGC TTT TCC CGC
Hprt1 reverse	TCA TCA TCA CTA ATC ACG ACG CTG G
Ets1 forward	CTC TCT GCT CCG CCA AGT G
Ets1 reverse	ACA GAG CGC AGC CCT AAA AT
Rnf167 forward	GCA CGC TCT ACG TGT CGA A
Rnf167 reverse	CAC CCC TAG GTC CCA CTT CT
Ndfip1 forward	CAC CAC CAG GAT GGA GGA AC
Ndfip1 reverse	CCC TTT TCA AAC AGC CAG CC
Ytk6 forward	TTC TCA AAG CCG CGT ACG AT
Ytk6 reverse	TTG GTC TCA TCC AGT TCG GC
Yeats2 forward	TTG GTC CAT GTA GCA GGT CG
Yeats2 reverse	CGT CCC AAT GAG CCC CTC TA
Parp9 forward	TTC TGT CTT CCG AGA CGC TG
Parp9 reverse	CAT CGG CTG GTC TTT CGG T
Pgr forward	GGC TGT CAC TAT GGT GTG CT
Pgr reverse	GTG TCG GGC TTT GTG TTG TC
Tenm4 forward	GCC GCA CAG GCA CTA ATT TC
Tenm4 reverse	GCT GGG ATG ATC GGT TTC G
Arc eRNA (+) forward	CCG GAG ACT GGT GAC ATT GC
Arc eRNA (+) reverse	CCC AGA ACT CGA GGG TAC AA
Arc eRNA (-) forward	TCT CCA TAG CAG GGG CAG TT
Arc eRNA (-) reverse	AGG ACC AGG ATA CAG GGA GAC
Chromatin Immunoprecipitation (ChIP)- PCR Primers	
Arc SARE forward	GCG TCA TGG CTC AGC TAT TC
Arc SARE reverse	GCT TCC GGC ACC ATA AAA GG
Arc TSS forward	AGT GCT CTG GCG AGT AGT CC
Arc TSS reverse	TCG GGA CAG GCT AAG AAC TC

Arc (-441 bp) forward	CAG GCA CTT CTG AGG TTG CA
Arc (-441 bp) reverse	GCT GAT GCG CCT ATC CTG A
Arc (-2868 bp) forward	GGG ACA CAC ACT GGT CTC AG
Arc (-2868 bp) reverse	TAC CCA AGG CTC TGG CCT AT
Ets1 forward	AAC ACT GCG GTT CAG GTA GG
Ets1 reverse	GAA CAA TGG CGT ATT GCG GG
Rnf167 forward	ATG AGG CCT CTC GCG GTA AT
Rnf167 reverse	GGT CCA AAA AGG CCG GTT GA
Ndfip1 forward	CAC GTC TGA GGA TGG CAG TT
Ndfip1 reverse	CAC TGA AGT CGT CTC CCT GC
Ytk6 forward	TCG ACG TTC ATG TGT GTG GT
Ytk6 reverse	CCA CAG TGC AAG GCA GTA GA
Yeats2 forward	TCT CCG AAG CTT CCA TAC GAC
Yeats2 reverse	CGC CTC GGC AAG TTT GGA TT
Parp9 forward	GGG CTG GAA TTG CTA CTG TCT
Parp9 reverse	GAC CTC GGT GGA CCG TTA TG
Pgr forward	AAG GTG AGG TAC AAA GTG GGT C
Pgr reverse	ACA GCA CTT TCT CAG ACG ACA T
Tenm4 forward	AGT GCA GAC AGT TCT CCA GC
Tenm4 reverse	TCT GTA GGT ACC CGG GAC TG
3C Primers	
Site 1	CCA GGC TCC TTG GCA AAA CAA A
Site 2	CTT CCC TGG ACA ACA CCT CTG T
Site 3	ACA CTG GGA AAG AGA AGC AGC A
Site 4	CCT CTG CAG AGC CTT CTT CTC C
SARE site	GGA CGT GGA CTA GCA CCA AGA T
Anchor Fragment	CTG GAG GTA GCA AGG GTG GAA A
Internal *Hprt1*	TCA GAG ACG CCA CGA ATC AG
Internal *Hprt1*	CCA GGC CCA ACT TGT CAG AA
Single guide (sg) RNAs sequence of *Arc* SARE site	
Arc SARE sgRNA1	GCG CGT AGA GCC TTC CTG CGT GG
Arc SARE sgRNA2	CGC GTA GAG CCT TCC TGC GTG GG
Arc SARE sgRNA3	AGC AAG GAG CTT CCC CAC GCA GG
Arc SARE sgRNA4	CTT GCT TCC GGC ACC ATA AAA GG

Table S2: Antibody information

Antigen	Isotype	ChIP	Confocal	Source and Catalog #	RRID#
H3K27me3	Rabbit IgG	3 µL	-	Active Motif 39155	AB_2561020
H3K27ac	Rabbit IgG	2 µL	-	Active Motif 39133	AB_2561016
H3K9me3	Rabbit IgG	3 µL	-	Active Motif 39765	AB_2793334
NELF-E	Mouse IgG	5 µL	-	Santa Cruz sc-377052	AB_2847957
Alexa Fluor® 488 Anti-CRISPR-Cas9 antibody [EPR18991]	Rabbit IgG	-	1:200	Abcam ab215239	AB_2892624
Anti-NeuN Antibody, clone A60	Mouse IgG	-	1:200	Millipore Sigma MAB377	AB_2298772
Alexa Fluor® 647AffiniPure Donkey Anti-Mouse IgG (H+L)	Mouse IgG	-	1:200	Jackson ImmunoResearch 715-605-151	AB_2340863

Table S3: Alcohol intake (g/kg) on each day by individual AIS and AIE adult rats infused with dCas9-P300 or dCas9-P300+ sgRNAs into CeA.

Ethanol Drinking (g/kg)															
Ethanol Concentration		3%			7%			9%							
Group	Animal	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
AIS + dCas9-P300	1	2.01	0.97	2.01	2.57	1.97	0.00	0.78	0.19	1.75	1.95	0.19	0.19	3.11	1.75
	2	1.68	1.36	0.84	0.60	1.06	4.37	1.16	0.58	1.16	0.78	0.78	2.13	3.30	1.94
	3	3.40	1.32	2.01	1.62	2.11	4.70	0.63	0.21	0.83	0.63	0.21	0.21	0.83	0.00
	4	3.01	1.62	2.16	2.16	2.34	3.60	0.00	0.46	0.69	0.69	0.69	0.23	1.39	0.46
	5	2.82	0.34	1.85	4.17	4.01	2.56	3.30	2.06	3.71	3.50	2.89	0.82	2.89	1.03
	Mean	2.58	1.12	1.77	2.22	2.30	3.05	1.17	0.70	1.63	1.51	0.95	0.72	2.30	1.04
	SEM	0.32	0.22	0.24	0.59	0.48	0.85	0.56	0.35	0.55	0.55	0.50	0.37	0.50	0.37
AIS + dCas9-P300 + sgRNAs	1	2.40	1.82	2.11	3.06	1.19	1.70	0.22	0.87	1.09	2.40	3.50	3.71	7.43	3.93
	2	2.86	1.00	2.00	4.84	0.17	0.33	1.50	4.50	5.36	2.14	3.00	0.64	3.22	2.57
	3	2.43	1.47	1.92	4.19	2.69	0.30	5.57	5.57	5.00	5.77	0.58	3.65	4.80	2.50
	4	1.06	1.06	2.05	1.39	3.86	1.24	3.18	2.38	5.56	4.17	1.99	2.18	3.97	2.18
	5	2.12	0.89	2.05	2.24	2.40	4.15	0.00	0.41	0.82	0.62	0.21	0.82	1.03	0.62
	6	2.67	1.80	1.86	2.61	1.89	3.92	0.56	0.37	1.49	1.12	0.19	1.49	0.75	0.19
	Mean	2.26	1.34	2.00	3.06	2.03	1.94	1.84	2.35	3.22	2.70	1.58	2.08	3.53	2.00
	SEM	0.26	0.17	0.04	0.52	0.52	0.70	0.88	0.91	0.94	0.79	0.60	0.55	1.02	0.56
AIE + dCas9-P300	1	3.29	2.45	2.80	6.53	6.37	8.00	9.66	7.56	7.98	8.61	6.30	6.09	7.98	8.40
	2	3.36	2.13	2.88	5.60	5.28	3.84	9.47	8.64	9.05	8.23	7.41	8.03	8.85	8.85
	3	1.89	1.89	2.39	5.57	5.87	5.87	5.09	4.53	6.22	7.92	5.09	5.28	7.92	5.28
	4	2.23	2.08	2.73	5.53	6.54	8.21	6.68	7.76	8.19	8.19	6.46	7.11	7.33	7.33
	5	2.52	1.70	2.66	7.08	6.74	8.46	6.00	6.22	6.66	7.11	6.22	6.88	7.11	6.66
	6	1.71	0.27	3.08	5.43	5.27	7.82	5.33	5.13	6.98	5.74	5.54	5.95	5.74	6.36
	Mean	2.50	1.75	2.76	5.96	6.01	7.03	7.04	6.64	7.51	7.63	6.17	6.56	7.49	7.15
	SEM	0.28	0.31	0.09	0.28	0.26	0.74	0.83	0.66	0.44	0.43	0.33	0.40	0.43	0.54
AIE + dCas9-P300 + sgRNAs	1	1.30	0.80	1.81	3.88	0.17	1.52	0.43	1.74	3.04	1.95	1.95	2.39	3.47	3.69
	2	2.49	1.38	1.44	4.13	0.15	5.20	0.20	0.59	0.79	0.20	0.00	2.95	0.59	1.18
	3	2.55	2.43	2.12	3.63	3.05	3.49	2.24	3.36	0.75	2.06	1.68	2.06	2.62	1.49
	4	2.75	0.85	1.91	3.29	0.00	3.95	0.21	0.42	0.42	0.21	0.21	1.06	0.42	0.64
	5	2.84	0.82	1.95	1.75	1.57	2.79	0.00	0.67	1.57	1.35	0.45	1.12	2.47	0.90
	6	1.81	0.08	1.73	2.99	2.64	0.00	0.23	0.90	0.23	1.58	0.90	2.71	1.13	0.23
	Mean	2.29	1.06	1.83	3.28	1.26	2.83	0.55	1.28	1.13	1.23	0.87	2.05	1.78	1.36
	SEM	0.25	0.32	0.09	0.35	0.55	0.75	0.34	0.46	0.42	0.34	0.33	0.33	0.51	0.50

Table S4: Sucrose intake (g/kg) on each day by individual AIS and AIE adult rats infused with dCas9-P300 or dCas9-P300+ sgRNAs into CeA.

Sucrose Drinking (g/kg)									
Sucrose Concentration		2%			4%				
Group	Animal	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
AIS + dCas9-P300	1	2.64	1.34	1.26	3.15	3.39	3.94	6.54	2.94
	2	3.05	2.89	1.74	5.79	5.23	5.39	9.20	5.51
	3	4.17	3.31	2.67	0.00	9.89	9.63	10.24	10.83
	4	2.70	1.62	2.56	4.23	5.90	5.01	6.78	4.01
	5	4.20	0.04	4.02	8.57	8.92	9.44	9.62	10.26
	Mean	3.35	1.84	2.45	4.35	6.67	6.68	8.48	6.71
	SEM	0.35	0.58	0.47	1.42	1.20	1.19	0.76	1.62
AIS + dCas9-P300 + sgRNAs	1	2.96	2.00	2.14	3.64	8.02	7.56	9.02	10.58
	2	3.35	1.79	0.00	8.75	9.02	6.88	10.09	10.01
	3	2.17	2.09	2.40	7.59	8.75	8.60	8.83	1.28
	4	3.24	2.15	2.19	8.24	9.51	9.76	10.01	9.71
	5	2.95	2.16	1.85	5.10	4.75	5.10	1.58	5.84
	6	3.76	3.52	2.63	7.59	8.75	6.20	8.36	7.96
	Mean	3.07	2.29	1.87	6.82	8.13	7.35	7.98	7.56
	SEM	0.22	0.25	0.39	0.82	0.70	0.68	1.31	1.44
AIE + dCas9-P300	1	4.16	3.00	2.19	8.41	9.70	10.21	10.13	0.65
	2	4.05	3.25	3.59	8.18	9.68	9.26	9.01	9.88
	3	2.14	1.80	3.71	2.83	6.95	5.50	8.56	4.36
	4	4.29	2.56	2.17	8.66	9.55	9.19	10.34	8.43
	5	2.69	1.81	1.95	4.64	4.64	5.10	10.12	6.61
	6	2.77	2.30	1.75	8.36	7.59	9.30	9.98	8.12
	Mean	3.35	2.45	2.56	6.85	8.02	8.09	9.69	6.34
	SEM	0.38	0.25	0.35	1.01	0.83	0.90	0.30	1.37
AIE + dCas9-P300 + sgRNAs	1	2.97	3.56	2.28	8.04	0.00	9.86	9.86	11.00
	2	3.54	0.04	4.04	8.16	11.07	10.49	9.82	9.96
	3	2.22	1.53	1.68	3.29	5.43	4.81	8.48	0.33
	4	4.10	2.75	3.36	8.56	9.87	0.44	9.52	0.09
	5	2.88	2.08	2.12	6.89	8.68	7.45	10.75	10.87
	6	4.64	4.35	3.92	8.03	10.80	10.51	11.85	11.35
	Mean	3.39	2.39	2.90	7.16	7.64	7.26	10.05	7.27
	SEM	0.36	0.62	0.41	0.81	1.74	1.64	0.47	2.24

Table S5: Alcohol intake (g/kg) on each day by individual alcohol naïve control adult rats infused with dCas9-KRAB or dCas9-KRAB+ sgRNAs into CeA.

Ethanol Drinking (g/kg)															
Ethanol Concentration		3%			7%			9%							
Group	Animal	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
dCas9-KRAB	1	1.91	1.11	1.03	0.74	3.90	1.30	2.86	1.19	2.15	0.95	1.19	1.19	3.10	0.72
	2	1.73	1.67	2.20	1.40	3.73	2.64	0.80	1.20	0.40	0.40	0.20	1.20	0.60	0.80
	3	2.13	2.05	2.99	2.19	4.78	0.60	0.51	5.37	4.61	3.07	4.09	1.79	1.02	3.07
	4	2.85	2.35	2.01	1.37	2.74	0.20	1.01	1.01	2.01	0.75	1.51	0.75	1.51	1.01
	5	2.16	1.64	3.29	1.01	0.00	0.20	0.00	1.30	0.26	1.30	0.52	0.26	0.78	0.78
	6	2.01	1.93	2.09	0.94	3.56	1.31	0.96	1.93	2.41	1.69	1.69	1.20	0.48	1.45
	Mean	2.13	1.79	2.27	1.28	3.12	1.04	1.02	2.00	1.97	1.36	1.53	1.07	1.25	1.31
	SEM	0.16	0.17	0.33	0.21	0.68	0.38	0.40	0.69	0.65	0.39	0.56	0.21	0.40	0.37
dCas9-KRAB + sgRNAs	1	1.61	1.70	2.04	4.36	3.97	3.37	5.86	3.82	5.61	3.31	4.08	6.12	4.84	2.29
	2	1.81	1.72	2.32	2.81	5.62	4.81	7.48	6.45	5.93	6.19	4.90	0.52	5.93	3.35
	3	1.78	2.04	1.95	4.56	4.16	4.76	6.37	6.88	5.86	6.37	6.12	6.12	5.86	5.35
	4	2.12	1.27	2.46	2.18	5.15	3.17	6.62	6.11	6.11	6.62	8.14	6.87	7.38	7.38
	5	1.59	1.91	1.67	1.30	3.71	1.86	2.63	4.30	3.10	3.10	2.15	3.82	2.15	0.24
	6	1.46	1.29	2.02	1.32	3.78	0.76	0.24	1.21	0.73	0.73	0.24	5.83	1.94	2.91
	7	1.52	1.90	1.83	4.26	4.62	3.02	6.62	3.43	6.40	5.48	6.17	5.25	6.62	5.71
	8	3.04	1.74	2.87	2.03	6.09	4.06	5.74	2.87	7.57	5.22	8.87	3.13	6.26	8.61
	Mean	1.87	1.70	2.15	2.85	4.64	3.23	5.20	4.38	5.16	4.63	5.08	4.71	5.12	4.48
	SEM	0.18	0.10	0.14	0.48	0.32	0.49	0.87	0.70	0.77	0.73	1.03	0.74	0.72	0.98

Table S6: Sucrose intake (g/kg) on each day by individual alcohol naive control adult rats infused with dCas9-KRAB or dCas9-KRAB+ sgRNAs into CeA.

Sucrose Drinking (g/kg)								
Sucrose Concentration		2%			4%			
Group	Animal	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
dCas9-KRAB	1	4.70	2.23	3.34	6.20	10.46	5.52	7.46
	2	3.14	2.32	1.49	4.84	5.35	4.02	4.02
	3	3.71	1.63	2.38	5.15	8.02	4.26	5.94
	4	5.78	5.61	5.45	0.11	12.96	2.05	10.58
	5	4.41	2.50	3.20	11.31	11.01	10.41	10.11
	Mean	4.35	2.86	3.17	5.52	9.56	5.25	7.62
	SEM	0.45	0.70	0.66	1.79	1.31	1.40	1.24
dCas9-KRAB + sgRNAs	1	3.70	2.76	4.07	3.23	10.64	5.63	11.16
	2	4.76	2.62	2.15	12.15	10.99	11.62	11.10
	3	2.57	1.85	2.05	1.03	6.37	6.98	6.78
	4	5.57	2.20	4.34	11.44	11.85	6.64	11.65
	5	2.92	1.56	2.83	8.09	8.09	4.48	9.26
	6	2.18	1.55	1.68	3.18	4.00	4.73	3.91
	7	6.01	3.72	5.43	11.81	0.00	10.96	10.96
	Mean	3.96	2.32	3.22	7.28	7.42	7.29	9.26
	SEM	0.57	0.29	0.53	1.79	1.63	1.09	1.10