Supplementary Table 1a. Quantitative input strengths of Camk2a-Cre SUB excitatory neurons versus CA1-projecting SUB excitatory neurons

Camk2a-Cre excitatory neurons	CA1 S.P.	CA1 S.O.	CA1 S.R.	CA1 S.L.M.	PrS	RSG	Vis Ctx	Au Ctx	TeA	PRh/ Ect	LEnt	mEnt	ACC	MS-DB	Thala-mus
Average CSI	47.72	0.90	0.14	0.17	1.16	0.46	0.74	0.51	0.38	0.39	0.53	0.46	0.09	0.75	0.30
SE	2.69	0.22	0.02	0.05	0.13	0.19	0.22	0.29	0.15	0.08	0.20	0.11	0.03	0.15	0.08
Average %	86.71	1.58	0.26	0.31	2.16	0.81	1.32	0.88	0.68	0.71	0.92	0.85	0.16	1.42	0.54
SE	1.56	0.36	0.03	0.09	0.35	0.30	0.35	0.46	0.26	0.12	0.30	0.22	0.06	21.34	0.15
# of starter	50 ± 8				**Total labeled neurons**			2681 ± 372				**N=5**			

CA1-projecting SUB neurons	CA1 S.P.	CA1 S.O.	CA1 S.R.	CA1 S.L.M.	PrS	RSG	Vis Ctx	Au Ctx	TeA	PRh/ Ect	LEnt	mEnt	ACC	MS-DB	Thala-mus
Average CSI	14.90	4.00	0.06	0.08	0.54	0.47	3.27	0.76	0.00	0.00	0.00	0.00	0.00	0.49	0.06
SE	1.25	0.44	0.06	0.08	0.15	0.26	0.55	0.36	0.00	0.00	0.00	0.00	0.00	0.17	0.06
Average %	60.28	16.19	0.21	0.41	2.20	2.01	13.18	2.88	0.00	0.00	0.00	0.00	0.00	1.99	0.21
SE	4.41	1.58	0.21	0.41	0.67	1.20	2.08	1.21	0.00	0.00	0.00	0.00	0.00	0.66	0.21
# of starter	3.2 ± 0.6				**Total labeled neurons**			77 ± 13				**N=6**			

Note: The input connection strength index (CSI) is defined as the ratio of the number of presynaptic neurons in a given brain structure versus the number of starter neurons. % is the percentage of the total input, which is defined as the number of labeled neurons in a given brain structure compared to the total number of labeled neurons. The local SUB input quantification is excluded. All data are presented as mean ± SE

Supplementary Table 1b. Statistic comparisons between input measurements of Camk2a-Cre SUB excitatory neuron and CA1-projecting SUB excitatory neuron

CSI	Comparisons of CSI, related to Figure2	Statistic Method	Significance	P value
	CA1 s.p.	t-test	***	9.13×10^{-7}
	CA1 s.o.	t-test	***	0.0002
	CA1 s.r.	t-test	ns	0.1873
	CA1 s.l.m	t-test	ns	0.4085
	PrS	t-test	*	0.0156
	RSG	t-test	ns	0.9823
	Visual Ctx	t-test	**	0.0032
	Auditory Ctx	t-test	ns	0.6044
	TeA	t-test	*	0.0239
	PRh/Ect	t-test	***	0.0004
	LEnt	t-test	*	0.0167
	mEnt	t-test	**	0.0013
	ACC	t-test	*	0.0175
	MS-DB	t-test	ns	0.3070
	AV Thalamus	t-test	*	0.0306
%	**Comparisons of % of total input**	**Statistic Method**	**Significance**	**P value**
	CA1 s.p.	t-test	***	0.0006
	CA1 s.o.	t-test	***	1.75×10^{-5}
	CA1 s.r.	t-test	ns	0.8087
	CA1 s.l.m	t-test	ns	0.8440
	PrS	t-test	ns	0.9580
	RSG	t-test	ns	0.4002
	Visual Ctx	t-test	***	0.0006
	Auditory Ctx	t-test	ns	0.1877
	TeA	t-test	*	0.0186
	PRh/Ect	t-test	***	0.0001
	LEnt	t-test	**	0.0083
	mEnt	t-test	**	0.0018
	ACC	t-test	*	0.0240
	MS-DB	t-test	ns	0.4935
	AV Thalamus	t-test	ns	0.2329

Supplementary Table 2a. Data for object-location and novel-object experiments with DREADDs-mediated inactivation of CA1-projecting subicular excitatory neurons

Object-location	Training (10 min)		Testing (5min)	
	Saline	CNO	Saline	CNO
Total Time (s)	20.83	20.67	8.24	7.40
SE	1.03	0.99	0.72	0.49
Discrimination Index (%)	0.51	-0.88	22.31	4.60
SE	2.24	1.04	3.16	2.82

Novel-object	Training (10 min)		Testing (5min)	
	Saline	CNO	Saline	CNO
Total Time (s)	21.27	21.69	7.92	9.70
SE	1.16	1.72	1.05	0.75
Discrimination Index (%)	-0.91	1.02	24.67	21.72
SE	2.24	0.72	5.22	6.30

Supplementary Table 2b. Training and Testing data for object-location memory enhancement experiments with activation of CA1-projecting subicular neurons via optogenetic stimulation

Object-location	Training (3 min)			Testing (5 min)		
	Laser + EGFP ctrl	No laser ctrl	Laser + ChR2	Laser + EGFP ctrl	No laser ctrl	Laser + ChR2
Total Time (s)	4.18	4.19	3.78	5.99	6.14	7.09
SE	0.46	0.42	0.25	0.47	0.75	0.72
Discrimination Index (%)	0.70	1.82	0.15	3.43	2.10	25.25
SE	3.25	2.02	1.95	3.10	4.54	4.69

Supplementary Table 3. Behavioral data of object-location memory experiments concurrent with miniscope imaging

Object-location tasks with miniscope imaging	Training (10 min)		Testing (10min)	
	Saline	CNO	Saline	CNO
Total Time (s)	8.76	9.06	8.70	9.18
SE	1.08	0.86	0.85	0.80
Discrimination Index (%)	-1.32	0.44	21.25	1.86
SE	1.51	1.28	2.58	2.37

Supplementary Table 4. Mouse strains and viral injections for the experiments

Mouse strain	Virus Injection	Target brain region	Experiments performed
Camk2a-Cre; TVA	AAV8-EF1a-FLEX-HB EnvA-SADΔG-mCherry	Subiculum (AP: -3.40 mm)*	Rabies tracing of inputs to subicular excitatory neurons (n = 5)
Ai9 (RCL-tdTomato)	CAV2-Cre	CA1 (AP: -1.94 mm)*	Verification of the efficiency and specificity of CAV2-Cre (n = 4)
C57BL/6	CAV2-Cre AAV8-EF1a-FLEX-HTB EnvA-SADΔG-mCherry	CA1 Subiculum	Rabies tracing of circuit inputs to CA1-projecting subicular excitatory neurons (n = 6)
C57BL/6	CAV2-Cre H129DTK-TT (HSV)	CA1 Subiculum	Anterograde HSV tracing of output projections of CA1-projecting subicular neurons (n = 5)
C57BL/6	AAV2/1-CAG-ChR2-Venus	Subiculum	ChR2 photoactivation mediated circuit mapping (n = 5)
C57BL/6	CAV2-Cre AAV2-DIO-hM4D-mCherry	CA1 Subiculum	Inactivation of CA1-projecting subicular neurons during object relocation (n = 21) and novel object recognition (n = 10) tasks, dry-land maze experiments (n = 10)
Camk2a-Cre	AAV2/1-CAG-ChR2-Venus / AAV2-DIO-hM4D-mCherry	Subiculum	In vitro validation of optogenetic stimulation (n = 4) or hM4D-CNO mediated neuronal inhibition (n = 4)
Ai32 (RCL-ChR2(H134R)/EYFP)	rAAV2-retro-hSyn-Cre	CA1	Optogenetic activation of CA1-projecting subicular neurons during object location memory training (n = 18)
C57BL/6	rAAV2-retro-hSyn-EGFP	CA1	GFP control for optogenetic activation during object location memory experiment (n = 8)
C57BL/6	CAV2-Cre AAV1-CamkII-GCaMP6f AAV2-DIO-hM4D-mCherry	CA1 CA1 (AP: -2.04 mm) Subiculum	Miniscope-based GCaMP6 imaging of CA1 place cells and genetic inactivation of CA1-projecting subicular neurons. Linear track (n = 9), open field (n = 8), object location memory (n = 21)

***** Standard anterior-posterior values relative to the bregma (see the Methods) are used for injections in CA1 and the subiculum, except otherwise specified. For all the experiments, mice at 8-12 weeks old (either sex) were used for surgeries and had free access

to food and water in their home-cages before and after surgeries. Please refer to the main text and online methods for more detailed information.