SUPPLEMENTAL MATERIAL

Table S1. Behavioral assessment of HDAC2 knockdown on functional recovery from stroke.

	Pre-operation			11 d after stroke			18 d after stroke			25 d after stroke		
		Stroke			Stroke			Stroke			Stroke	
	Sham	LV-GFP	LV-HDAC2-shRNA-GFP	Sham	LV-GFP	LV-HDAC2-shRNA-GFP	Sham	LV-GFP	LV-HDAC2-shRNA-GFP	Sham	LV-GFP	LV-HDAC2-shRNA-GFP
	(n =10)	(n =13)	(n =13)	(n =10)	(n =13)	(n =13)	(n =10)	(n =13)	(n =13)	(n =10)	(n =13)	(n =13)
Foot faults relative to total steps taken (%) [*forelimb*]	7.80 ± 0.47	8.19 ± 0.43	7.50 ± 0.53	8.24 ± 0.73	28.47 ± 1.81	18.40 ± 1.64	8.19 ± 0.43	25.14 ± 0.89	17.43 ± 1.67	8.11 ± 0.63	23.98 ± 1.30	16.22 ± 0.72
Foot faults relative to total steps taken (%) [*hindlimb*]	1.86 ± 0.63	1.78 ± 0.50	1.81 ± 0.50	1.99 ± 0.69	6.65 ± 0.27	3.59 ± 0.60	1.70 ± 0.60	5.91 ± 0.17	3.55 ± 0.84	1.41 ± 0.74	6.28 ± 0.39	2.91 ± 0.67
Time spent on right paw relative to left (%)	0.57 ± 1.25	0.20 ± 1.06	0.32 ± 0.95	0.24 ± 0.96	25.41 ± 2.81	16.60 ± 1.54	0.87 ± 0.51	23.55 ± 2.22	15.93 ± 1.82	0.77 ± 0.81	18.04 ± 2.18	10.92 ± 1.54

Table S2. Behavioral assessment of HDAC2 over-expression on functional recovery from stroke.

	Pre-operation			11 d after stroke			18 d after stroke			25 d after stroke		
		Stroke			Stroke			Stroke			Stroke	
	Sham	Ad-inactive-HDAC2-Flag	Ad-HDAC2-Flag	Sham	Ad-inactive-HDAC2-Flag	Ad-HDAC2-Flag	Sham	Ad-inactive-HDAC2-Flag	Ad-HDAC2-Flag	Sham	Ad-inactive-HDAC2-Flag	Ad-HDAC2-Flag
	(n =10)	(n =13)	(n =13)	(n =10)	(n =13)	(n =13)	(n =10)	(n =13)	(n =13)	(n =10)	(n =13)	(n =13)
Foot faults relative to total steps taken (%) [*forelimb*]	7.84 ± 0.71	7.28 ± 0.52	8.06 ± 0.54	8.22 ± 0.75	18.94 ± 0.70	30.06 ± 1.19	8.27 ± 0.65	16.86 ± 0.89	26.73 ± 1.15	6.58 ± 0.62	14.53 ± 0.75	19.59 ± 0.61
Foot faults relative to total steps taken (%) [*hindlimb*]	1.85 ± 0.26	1.68 ± 0.38	1.70 ± 0.25	1.33 ± 0.24	4.24 ± 0.26	7.18 ± 1.19	1.83 ± 0.29	4.31 ± 0.83	7.47 ± 0.53	1.69 ± 0.30	3.99 ± 0.28	6.69 ± 0.90
Time spent on right paw relative to left (%)	0.01 ± 0.93	0.07 ± 0.70	0.24 ± 1.20	0.27 ± 0.36	18.42 ± 1.56	26.06 ± 2.64	0.03 ± 1.50	12.62 ± 1.33	20.04 ± 2.33	0.05 ± 0.79	11.24 ± 1.60	16.07 ± 1.01

Table S3. Behavioral assessment of TSA on functional recovery from stroke in WT mice.

	Pre-operation			11 d after stroke			18 d after stroke			25 d after stroke		
		Stroke			Stroke			Stroke			Stroke	
WT	Sham (n = 7)	Vehicle (n = 7)	TSA (n = 7)	Sham (n = 7)	Vehicle (n = 7)	TSA (n = 7)	Sham (n = 7)	Vehicle (n = 7)	TSA (n = 7)	Sham (n = 7)	Vehicle (n = 7)	TSA (n = 7)
Foot faults relative to total steps taken (%) [*forelimb*]	9.14 ± 1.08	9.35 ± 0.32	8.94 ± 0.45	9.45 ± 0.73	27.14 ± 1.79	19.53 ± 1.49	9.70 ± 0.48	24.79 ± 1.09	17.21 ± 0.62	9.14 ± 0.25	21.40 ± 0.96	15.12 ± 0.53
Foot faults relative to total steps taken (%) [*hindlimb*]	2.05 ± 1.06	2.10 ± 0.89	2.01 ± 0.48	1.98 ± 0.25	6.28 ± 0.40	3.84 ± 0.25	2.25 ± 0.50	5.38 ± 0.34	3.33 ± 0.25	1.83 ± 0.60	5.20 ± 0.39	2.75 ± 0.37
Time spent on right paw relative to left (%)	0.53 ± 0.20	0.24 ± 0.61	0.61 ± 0.24	1.76 ± 0.79	30.10 ± 3.43	17.37 ± 1.16	0.35 ± 0.13	25.76 ± 2.13	16.82 ± 0.78	0.62 ± 0.55	24.44 ± 2.06	13.82 ± 1.01

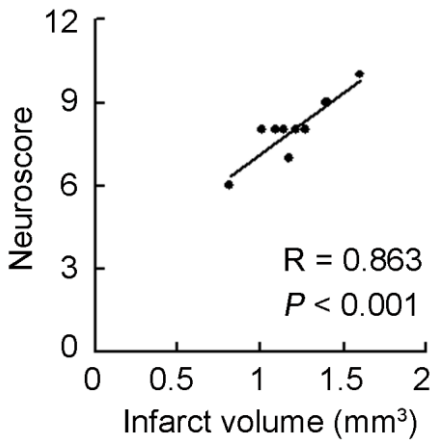
Table S4. Behavioral assessment of TSA on functional recovery from stroke in *Hdac2* CKO mice.

	Pre-operation			11 d after stroke			18 d after stroke			25 d after stroke		
		Stroke			Stroke			Stroke			Stroke	
Hdac2 CKO	Sham (n = 7)	Vehicle (n = 7)	TSA (n = 7)	Sham (n = 7)	Vehicle (n = 7)	TSA (n = 7)	Sham (n = 7)	Vehicle (n = 7)	TSA (n = 7)	Sham (n = 7)	Vehicle (n = 7)	TSA (n = 7)
Foot faults relative to total steps taken (%) [*forelimb*]	9.51 ± 0.60	9.01 ± 0.50	8.49 ± 0.29	9.96 ± 0.32	20.05 ± 1.16	20.92 ± 0.71	8.87 ± 0.27	16.62 ± 1.19	17.03 ± 1.19	9.71 ± 0.53	15.84 ± 0.73	14.53 ± 0.64
Foot faults relative to total steps taken (%) [*hindlimb*]	1.72 ± 0.33	2.05 ± 0.40	1.85 ± 0.33	1.90 ± 0.48	3.68 ± 0.36	3.73 ± 0.83	1.92 ± 0.19	3.11 ± 0.47	3.92 ± 0.46	1.98 ± 0.53	2.93 ± 0.38	3.04 ± 0.47
Time spent on right paw relative to left (%)	0.77 ± 0.56	1.46 ± 0.70	0.61 ± 0.54	0.61 ± 0.44	14.06 ± 2.64	15.66 ± 1.56	0.37 ± 0.20	15.39 ± 3.04	14.01 ± 1.36	1.09 ± 0.75	14.67 ± 1.54	13.58 ± 1.22

Table S5. Behavioral assessment of SAHA on functional recovery from stroke.

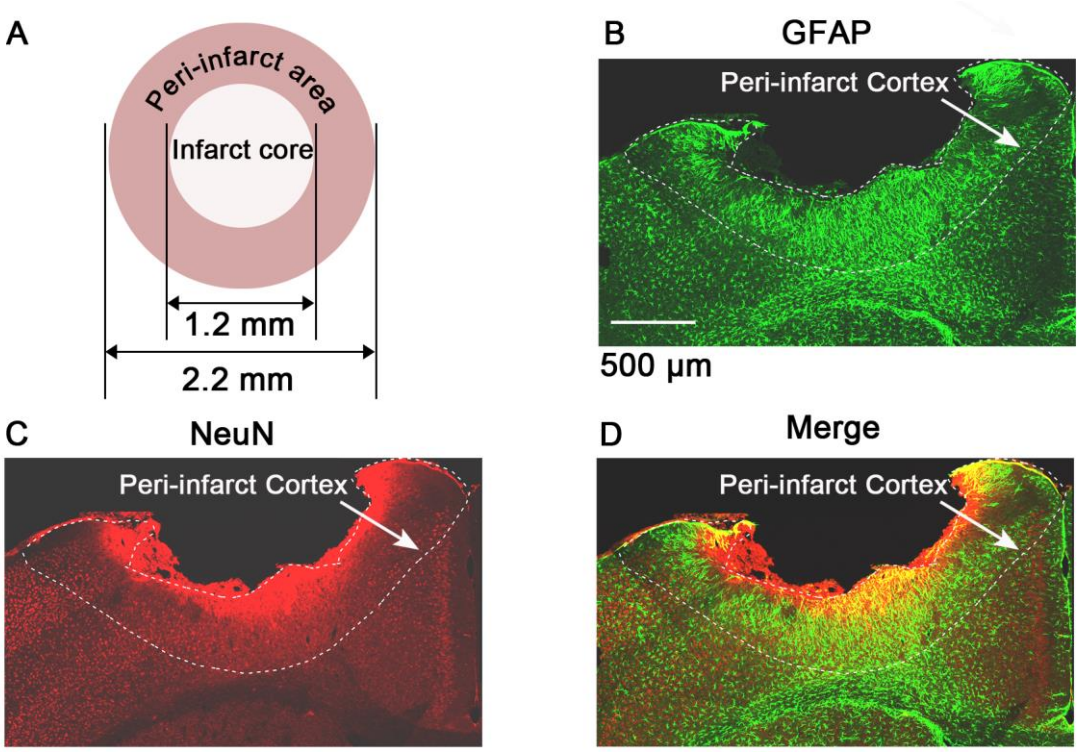
	Pre-operation			11 d after stroke			18 d after stroke			25 d after stroke		
		Stroke			Stroke			Stroke			Stroke	
	Sham (n =10)	Vehicle (n =13)	SAHA (n =13)	Sham (n =10)	Vehicle (n =13)	SAHA (n =13)	Sham (n =10)	Vehicle (n =13)	SAHA (n =13)	Sham (n =10)	Vehicle (n =13)	SAHA (n =13)
Foot faults relative to total steps taken (%) [*forelimb*]	6.69 ± 0.45	6.62 ± 0.63	7.13 ± 0.58	8.29 ± 0.38	25.68 ± 1.50	18.39 ± 0.75	7.63 ± 0.53	23.52 ± 1.74	17.28 ± 0.64	7.25 ± 0.44	21.65 ± 1.64	16.24 ± 0.91
Foot faults relative to total steps taken (%) [*hindlimb*]	2.05 ± 0.39	1.89 ± 0.52	1.78 ± 0.32	1.38 ± 0.59	8.04 ± 0.86	4.05 ± 0.69	1.41 ± 0.58	7.82 ± 1.15	4.12 ± 0.81	1.82 ± 0.54	7.71 ± 0.89	4.29 ± 1.01
Time spent on right paw relative to left (%)	0.51 ± 0.99	0.12 ± 0.98	0.33 ± 0.76	0.08 ± 0.98	29.92 ± 3.31	19.06 ± 3.20	0.27 ± 0.85	26.14 ± 3.89	16.07 ± 1.64	0.16 ± 0.62	23.05 ± 2.18	13.40 ± 1.50

Figure S1. Scatterplot for correlation between neuroscore and lesion size after stroke



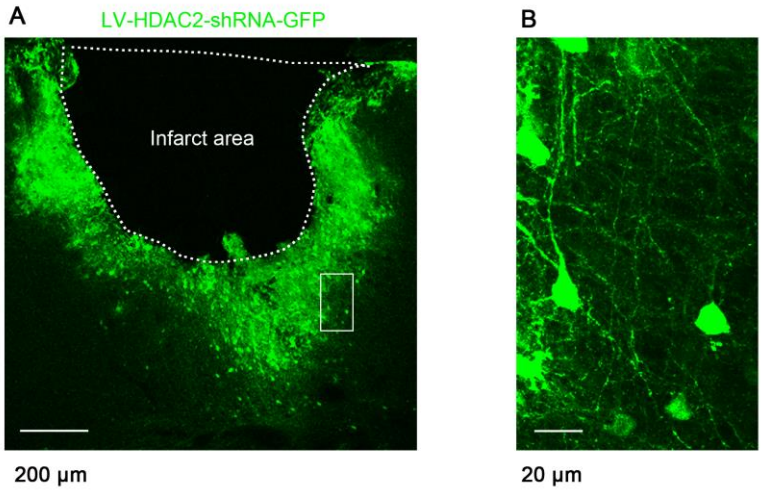
(n = 12, R = 0.863, $P < 0.001$)**.**

Figure S2. Diagram and immunostaining showing peri-infarct cortex.



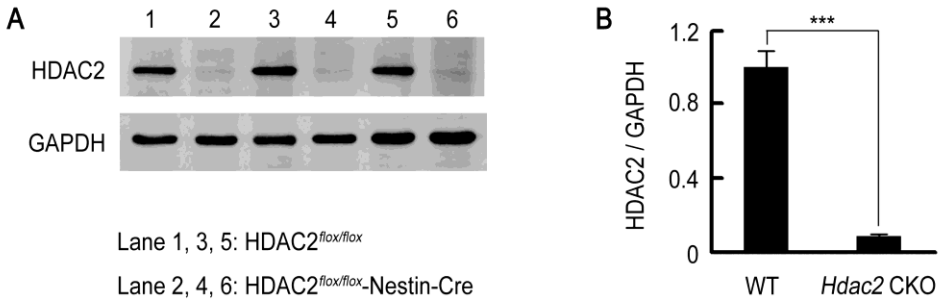
(A) The diagram showing the definition of the peri-infarct cortex for immunoblots. (B) Representative images of immunohistochemical labeling of NeuN, a transcription factor that is expressed in mature neurons. Scale bar, 500 μm. (C) Representative images of immunohistochemical labeling of GFAP, a marker of astrocytes. (D) The merged image from (B) and (C) showing the peri-infarct area. In the peri-infarct cortex, activated astrocytes were radiately distributed. GFAP, glial fibrillary acidic protein.

Figure S3. Confirmation of LV-HDAC2-shRNA-GFP infection.



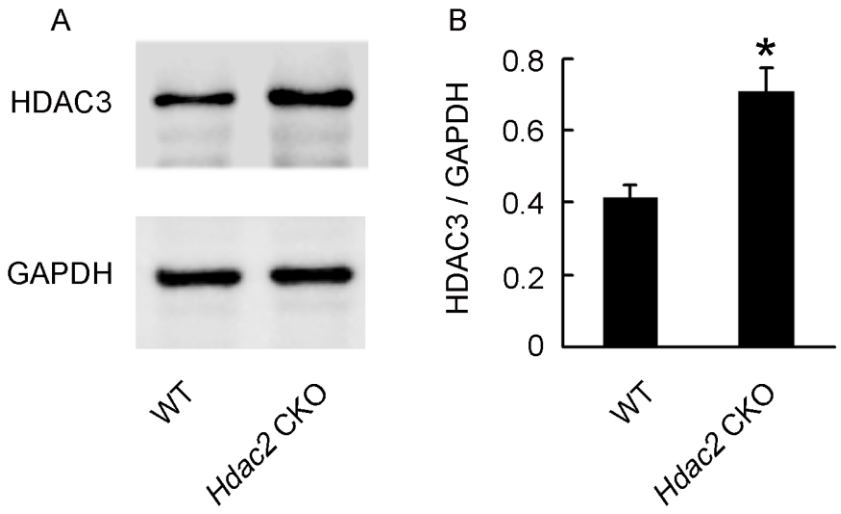
(A) A representative image showing LV-HDAC2-shRNA-GFP-infected peri-infarct cortex. (B) A high-magnification image from a selected area in leftward image. LV, lentivirus; HDAC2, histone deacetylase 2; shRNA, short hairpin RNA; GFP, green fluorescent protein.

Figure S4. Elimination of HDAC2 protein expression in the cortex is demonstrated by Western analysis.



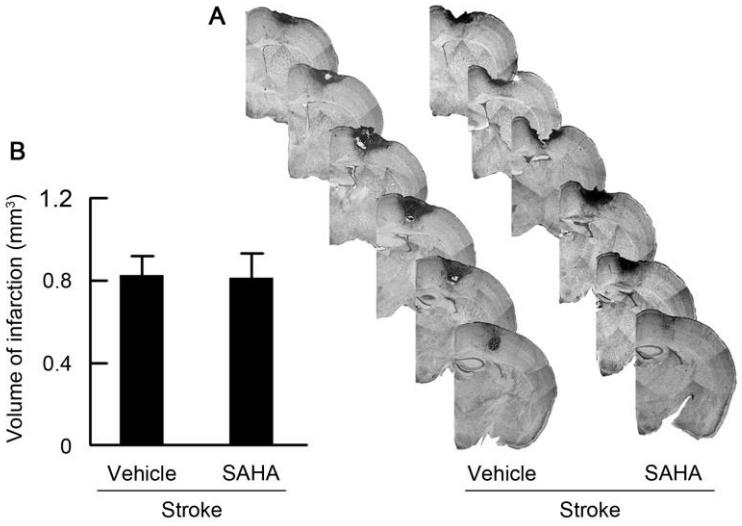
(A) Immunoblots showing HDAC2 levels in the cortex of HDAC2$^{flox/flox}$-Nestin-Cre and control HDAC2$^{flox/flox}$ mice. (B) Bar graph showing cortex HDAC2 level of *Hdac2* CKO mice and WT littermates (n = 3, two-tailed *t test*, $^{***}P < 0.001$). HDAC2, histone deacetylase 2; *Hdac*2 CKO, *Hdac2* conditional knockout; WT, wild type.

Figure S5. *Hdac*2 CKO leads to compensatory up-regulation of HDAC3.



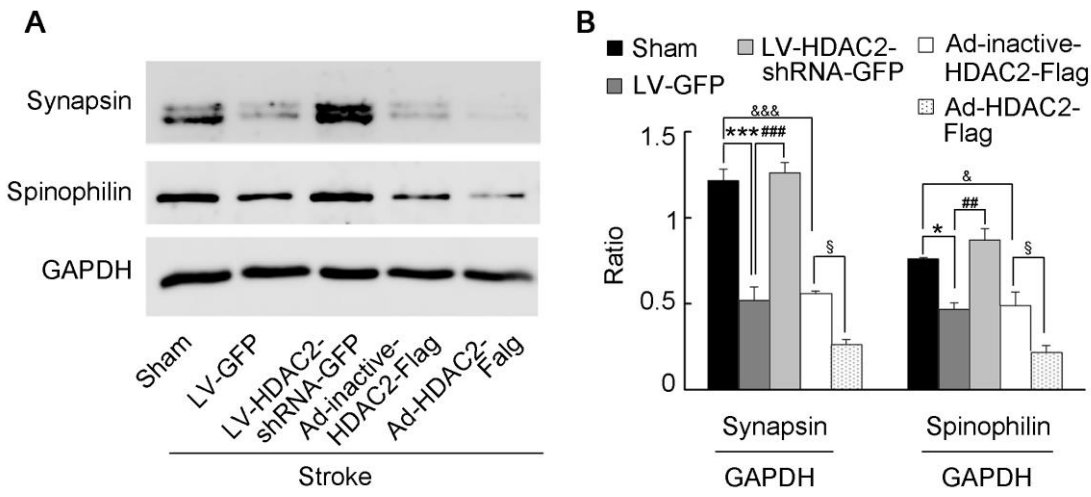
(A) Immunoblots showing HDAC3 levels in the cortex of WT and *Hdac2* CKO mice. (B) Bar graph showing cortex HDAC3 level of *Hdac2* CKO mice and WT littermates (n = 3, two-tailed *t test*, $^{*}P < 0.05$). *Hdac*2 CKO, *Hdac2* conditional knockout; HDAC3, histone deacetylase 3; WT, wild type.

Figure S6. Administration of SAHA during 4-10 d after stroke has no effect on infarct size.



(A) Representative Nissl-stained sections at 11 d after stroke from stroke + vehicle and stroke + SAHA, respectively. (B) Bar graph showing stroke volume from stroke+vehicle and stroke + SAHA, respectively (n = 8, two tailed *t test*, $P > 0.05$). SAHA, suberoylanilide hydroxamic acid.

Figure S7. HDAC2 knockdown reversed, whereas HDAC2 over-expression further augmented stroke-induced down-regulation of neuroplasticity-related proteins.



(A) Representative immunoblots and (B) Bar graph showing levels of Synapsin and Spinophilin in the peri-infarct cortex after stroke (n = 4, one-way ANOVA, $^{*}P < 0.05$, $^{***}P < 0.001$, LV-GFP vs sham; $^{\#\#}P < 0.01$, $^{\#\#\#}P < 0.001$, LV-HDAC2-shRNA-GFP vs LV-GFP; $^{\&}P < 0.05$, $^{\&\&\&}P < 0.001$, Ad-inactive-HDAC2-Flag vs sham; $^{\S}P < 0.05$, Ad-HDAC2-Flag vs Ad-inactive-HDAC2-Flag). HDAC2, histone deacetylase 2; LV, lentivirus; shRNA, short hairpin RNA; GFP, green fluorescent protein; Ad, adenovirus.