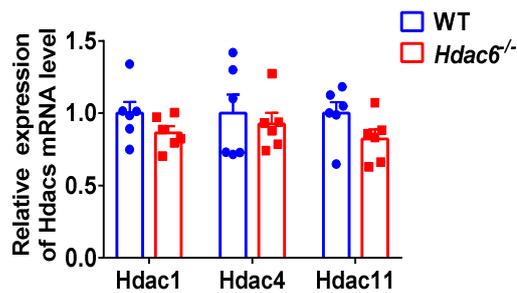
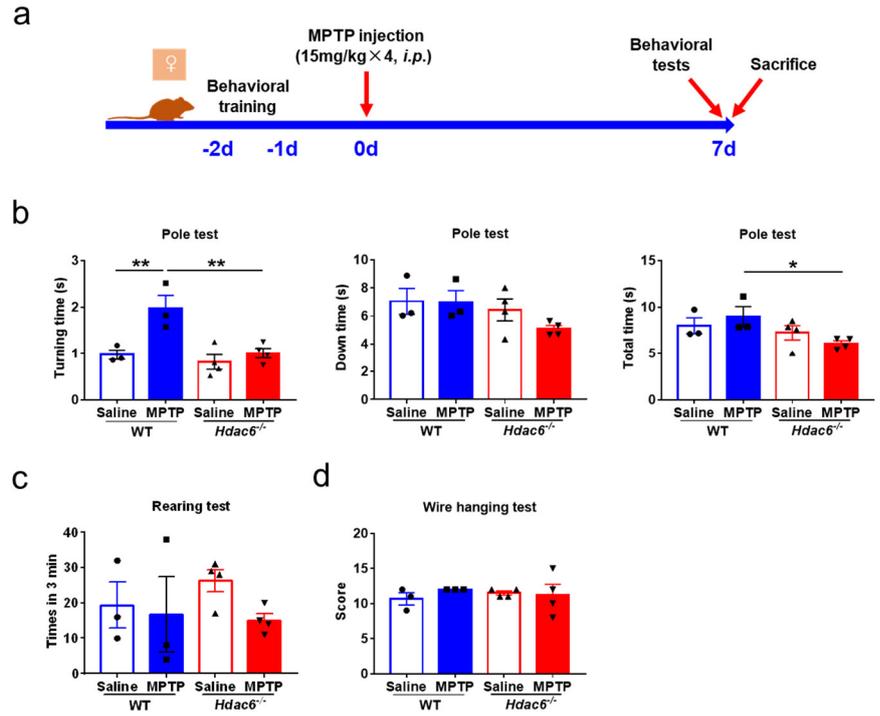


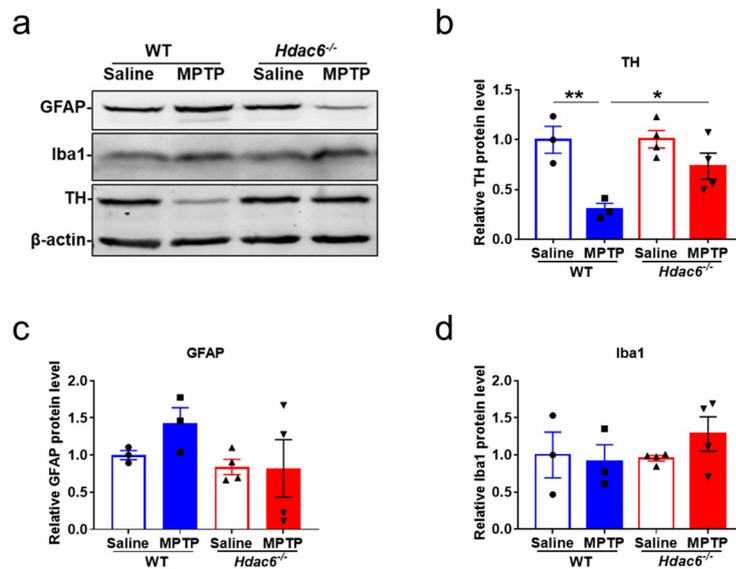
**Figure S1.** The targeting strategy and validation of HDAC6 deficiency in mice. (a) The construction strategy of *Hdac6*<sup>-/-</sup> mice. (b) Genotyping of *Hdac6*<sup>-/-</sup> mice. PCR primers used are indicated as primers I, II, IV. (c) Verification of HDAC6 deficiency in the brain of *Hdac6*<sup>-/-</sup> mice by qPCR. n=5-6. (d) Verification of HDAC6 deficiency in the brain of *Hdac6*<sup>-/-</sup> mice by Western blot. (e) The effect of HDAC6 deficiency on the acetylation of  $\alpha$ -tubulin in the striatum of mice. n=6, \**p* < 0.05.



**Figure S2.** The transcripts of *Hdac1*, *Hdac4* and *Hdac11* in the brain of WT and *Hdac6*<sup>-/-</sup> mice detected by qPCR. n=6.



**Figure S3.** The effects of HDAC6 loss on PD-related motor injuries induced by MPTP injection in female WT and *Hdac6*<sup>-/-</sup> mice. **(a)** The experimental schedule. **(b, c, d)** PD-related behavioral tests were performed in mice at 7 days after the last injection of MPTP or NS. **(b)** The results of pole test. **(c)** The results of rearing test. **(d)** The results of wire hanging test. *n*=3-4, \**p* < 0.05, \*\**p* < 0.01.



**Figure S4.** The impact of HDAC6 deficiency on MPTP-induced changes in the striatum of female WT and *Hdac6*<sup>-/-</sup> mice at 7 days after MPTP administration. **(a)** Representative western blot of striatal TH, GFAP and Iba1 proteins,  $\beta$ -actin served as the control. **(b-d)** Quantification of TH protein levels **(b)**, GFAP protein levels **(c)**, and Iba1 protein levels **(d)**. *n*=3-4, \**p* < 0.05, \*\**p* < 0.01.

## Supplementary Table

Table S1. The main results

Direction	Index	Male				Female			
		WT		<i>Hdac6</i> <sup>-/-</sup>		WT		<i>Hdac6</i> <sup>-/-</sup>	
		Saline	MPTP	Saline	MPTP	Saline	MPTP	Saline	MPTP
Behaviors	Motor activity		○	↑	○		○	↓	○
	Anxiety or depression		○	↑	○		○	↓	○
PD-related behaviors	Motor ability		↓	-	-↑		↓	-	-↑
	Limb strength		↓	-	-		-	-	-
DA system	Striatal TH proteins		↓	-	↓		↓	-	-↑
Inflammation	Activation of astrocyte in SNpc (7d)		↑	-	↑		○	○	○
	Activation of microglia in SNpc (3d)		↑	-	↑		○	○	○
	Activation of astrocyte in striatum (7d)		↑	-	-		-	-	-
	Activation of microglia in striatum (3d)		↑	-	-		- (7d)	- (7d)	- (7d)

↑ ↓: enhancement or reduction vs. respective saline control; ↑ ↓: enhancement or reduction vs. WT saline control;

↑ : enhancement vs. WT MPTP group; - : no change vs. respective saline control; - : no change vs. WT saline control;

○: not tested.