Inhibition of HDAC increases BDNF expression and promotes neuronal rewiring and functional recovery after brain injury

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Brain injury causes serious motor, sensory, and cognitive disabilities. Accumulating evidence has demonstrated that histone deacetylase (HDAC) inhibitors exert neuroprotective effects against various insults to the central nervous system (CNS). In this study, we investigated the effects of the class I HDAC inhibition on the expression of brain-derived neurotrophic factor (BDNF) and functional recovery after traumatic brain injury (TBI) in mice. Knockdown of HDAC2 in cultured neurons increased the number of synaptic puncta. Administration of class I HDAC inhibitor CI-994 increased the number of synaptic boutons in rewiring corticospinal fibers and improved the recovery of motor functions after TBI. HDAC2 was mainly expressed in neurons and was increased in the premotor spinal interneurons, followed by decrease of BDNF expression in TBI. Knockdown of HDAC2 elevated H4K5ac enrichment at the BDNF promoter and increased BDNF expression after TBI. Together, our findings suggest that HDAC inhibition increases expression of neurotrophic factors, and promote neuronal rewiring and functional recovery following TBI.