Carbonic anhydrase 4

Cocaine use followed by withdrawal induces synaptic changes in the nucleus accumbens (NAc), which are thought to underlie subsequent drug-seeking behaviors and relapse. Previous studies suggest that cocaine-induced synaptic changes depend on acid-sensing ion channels (ASICs). Gupta et al. investigated the potential involvement of carbonic anhydrase 4 (CA4), an extracellular pH-buffering enzyme. They examined the effects of CA4 in mice on ASIC-mediated synaptic transmission in medium spiny neurons (MSNs) in NAc, as well as on cocaine-induced synaptic changes and behavior. They found that CA4 is expressed in the NAc and present in synaptosomes. Disrupting CA4 either globally, or locally, increased ASIC-mediated synaptic currents in NAc MSNs and protected against cocaine withdrawal-induced changes in synapses and cocaine-seeking behavior. These findings raise the possibility that CA4 might be a previously unidentified therapeutic target for addiction and relapse [1].

1)
Gupta SC, Ghobbeh A, Taugher-Hebl RJ, Fan R, Hardie JB, LaLumiere RT, Wemmie JA. Carbonic anhydrase 4 disruption decreases synaptic and behavioral adaptations induced by cocaine withdrawal. Sci Adv. 2022 Nov 18;8(46):eabq5058. doi: 10.1126/sciadv.abq5058. Epub 2022 Nov 16. PMID: 36383659.