

# Cocaine withdrawal

**Cocaine withdrawal** occurs when someone who has used a lot of **cocaine** cuts down or quits taking the drug.

Cocaine use followed by **withdrawal** induces **synaptic plasticity** 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 <sup>1)</sup>.

<sup>1)</sup>

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.

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