Acid sensing ion channels

Acid-sensing ion channels (ASICs) are neuronal ion-permeable channels activated by H+. These receptors are thought to play a role in anxiety disorders associated with changes in acidosis in the brain and blood, such as during panic attacks.

Persons at risk for developing alcohol use disorder (AUD) differ in their sensitivity to acute alcohol intoxication. Alcohol effects are complex and are thought to depend on multiple mechanisms. Harmata et al. explored whether acid-sensing ion channels (ASICs) might play a role. They tested ASIC function in transfected CHO cells and amygdala principal neurons and found alcohol-potentiated currents mediated by ASIC1A homomeric channels, but not ASIC1A/2 A heteromeric channels. Supporting a role for ASIC1A in the intoxicating effects of alcohol in vivo, they observed marked alcohol-induced changes on local field potentials in the basolateral amygdala, which differed significantly in Asic1a-/- mice, particularly in the gamma, delta, and theta frequency ranges. Altered electrophysiological responses to alcohol in mice lacking ASIC1A, were accompanied by changes in multiple behavioral measures. Alcohol administration during amygdala-dependent fear conditioning dramatically diminished context and cue-evoked memory on subsequent days after the alcohol had cleared. There was significant alcohol-by-genotype interaction. Context- and cue-evoked memory were notably worse in Asic1a-/- mice. They further examined the acute stimulating and sedating effects of alcohol on locomotor activity, loss of righting reflex, and an acute intoxication severity scale. They found loss of ASIC1A increased the stimulating effects of alcohol and reduced the sedating effects compared to wild-type mice, despite similar blood alcohol levels. Together these observations suggest a novel role for ASIC1A in the acute intoxicating effects of alcohol in mice. They further suggest that ASICs might contribute to the intoxicating effects of alcohol and AUD in humans [1)]

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Harmata GIS, Chan AC, Merfeld MJ, Taugher-Hebl RJ, Harijan AK, Hardie JB, Fan R, Long JD, Wang GZ, Dlouhy BJ, Bera AK, Narayanan NS, Wemmie JA. Intoxicating effects of alcohol depend on acid-sensing ion channels. Neuropsychopharmacology. 2022 Oct 15. doi: 10.1038/s41386-022-01473-4. Epub ahead of print. PMID: 36243771.