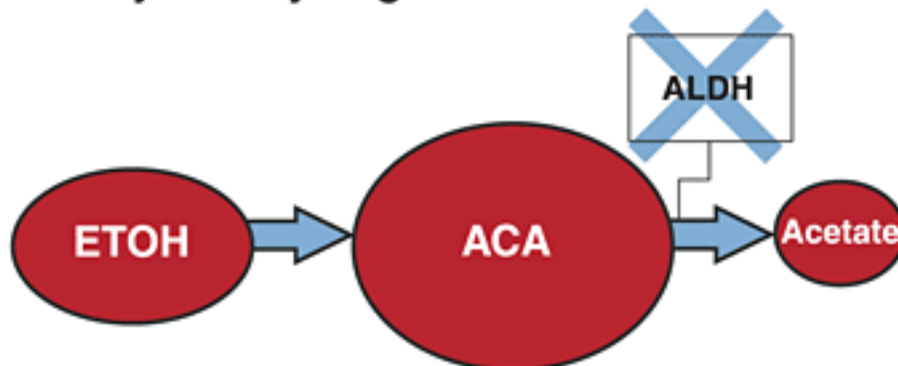


Schematic representation of the metabolism of ethanol (ETOH) and the effects of aldehyde dehydrogenase (ALDH) inhibitors and catalase modulators

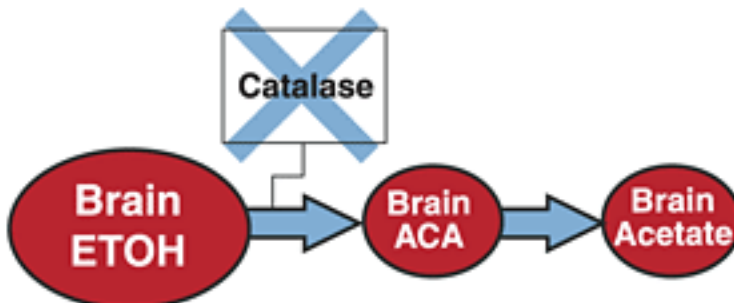
Normal metabolism



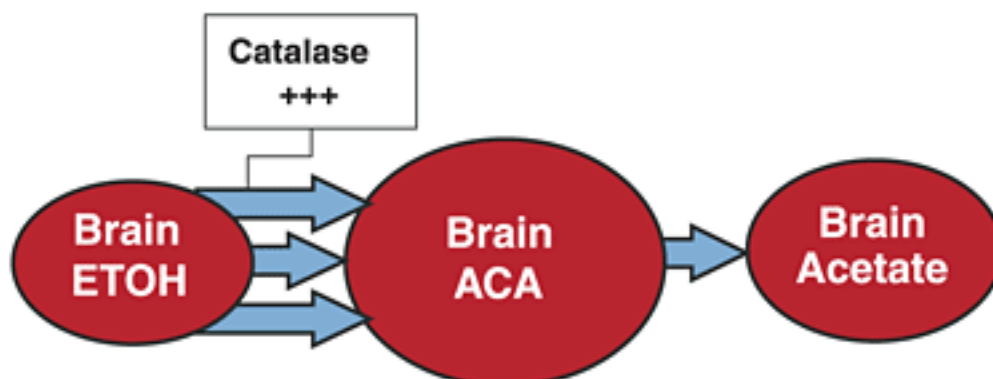
Aldehyde dehydrogenase inhibition



Catalase inhibition



Catalase activation



Under normal physiological conditions, ethanol is metabolized to acetaldehyde (ACA) through several enzymatic pathways involving alcohol dehydrogenase (ADH), cytochrome P4502E1 (CYP2E1), or catalase. When ALDH is pharmacologically inhibited, acetaldehyde accumulates to high concentrations both in the brain and in the periphery. Catalase metabolizes about 60 percent of ethanol in the brain. Therefore, inhibition of catalase is believed to reduce brain acetaldehyde levels, whereas enhancement of catalase activity is believed to increase brain acetaldehyde levels.