Activation of mitochondrial aldehyde dehydrogenase (ALDH2) by ALDA-1 reduces both the acquisition and maintenance of ethanol intake in rats: A dual mechanism?

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 A number of pre-clinical studies have shown that brain-generated acetaldehyde, the first metabolite of ethanol, exerts reinforcing effects that promote the acquisition of ethanol intake, while chronic intake maintenance appears to be mediated by alcohol-induced brain neuroinflammation/oxidative stress. Recently, it was described that N-(1,3-benzodioxol-5-ylmethyl)-2,6-dichlorobenzamide (ALDA-1) activates aldehyde dehydrogenase-2 (ALDH2), enzyme that catalyzes the oxidation of ethanol-derived acetaldehyde to acetate. The aim of this study was to determine the effects of ALDA-1 on both the acquisition and the maintenance of alcohol intake in alcohol-preferring UChB rats. For ethanol acquisition studies, naïve UChB rats were treated with five daily doses of ALDA-1 (12.5, 25 or 50 mg/kg, i.p.) from one day before the start of ethanol exposure. For chronic intake studies, UChB rats exposed for 98 days to a free access to 10% ethanol and water were treated daily with ALDA