

Long-term inhibition of ethanol intake by the administration of an aldehyde dehydrogenase-2 (ALDH2)-coding lentiviral vector into the ventral tegmental area of rats

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Previous studies suggest that acetaldehyde generated from ethanol in the brain is reinforcing. The present studies tested the feasibility of achieving a long-term reduction of chronic and post-deprivation binge ethanol drinking by a single administration into the brain ventral tegmental area (VTA) of a lentiviral vector that codes for aldehyde dehydrogenase-2 (ALDH2), which degrades acetaldehyde. The ALDH2 gene coding vector or a control lentiviral vector were microinjected into the VTA of rats bred for their alcohol preference. In the chronic alcohol administration model, naïve animals administered the control vector and subsequently offered 10% ethanol and water ingested 8-9-g ethanol/kg body weight/day. The single administration of the ALDH2-coding vector prior to allowing ethanol availability reduced ethanol drinking by 85-90% ($P < 0.001$) for the 45 days tested. In the post-deprivation binge-drinking model, animals that had previously consumed ethanol chronically for 81 days were administered the lentiviral vector and were thereafter deprived of ethanol for three 7-day periods, each interrupted by a single 60-minute ethanol re-access after the last day of each deprivation period. Upon ethanol re-access, control vector-treated animals consumed intoxicating 'binge' amounts of ethanol, reaching intakes of 2.7-g ethanol/kg body weight in 60 minutes. The administration of the ALDH2-coding vector reduced re-access binge drinking by 75-80% ($P < 0.001$). This study shows that endowing the ventral tegmental with an increased ability to degrade acetaldehyde greatly reduces chronic alcohol consumption and post-deprivation binge

drinking for prolonged periods and supports the hypothesis that brain-generated acetaldehyde promotes alcohol drinking. © 2014 Society for the Study of Addiction.

Acetaldehyde

ADE

chronic ethanol intake

lentiviral vector

VTA

acetaldehyde

aldehyde dehydrogenase isoenzyme 2

lentivirus vector

aldehyde dehydrogenase

Aldh2 protein, rat

mitochondrial protein

alcohol consumption

alcohol withdrawal

animal experiment

animal model

Article

binge drinking

comparative study

controlled study

drinking behavior

enzyme activity

genetic code

HEK293 cell line

nonhuman

priority journal

rat

ventral tegmentum

alcoholism

animal

drug seeking behavior

gene vector

genetics

Lentivirinae

metabolism

reinforcement

ventral tegmentum

Acetaldehyde

Alcohol Drinking

Alcoholism

Aldehyde Dehydrogenase

Animals

Binge Drinking

Drug-Seeking Behavior

Genetic Vectors

Lentivirus

Mitochondrial Proteins

Rats

Reinforcement (Psychology)

Ventral Tegmental Area