

The "first hit" toward alcohol reinforcement: Role of ethanol metabolites

Israel Y.

Quintanilla M.E.

Karahanian E.

Rivera-Meza M.

Herrera-Marschitz M.

This review analyzes literature that describes the behavioral effects of 2 metabolites of ethanol (EtOH): acetaldehyde and salsolinol (a condensation product of acetaldehyde and dopamine) generated in the brain. These metabolites are self-administered into specific brain areas by animals, showing strong reinforcing effects. A wealth of evidence shows that EtOH, a drug consumed to attain millimolar concentrations, generates brain metabolites that are reinforcing at micromolar and nanomolar concentrations. Salsolinol administration leads to marked increases in voluntary EtOH intake, an effect inhibited by mu-opioid receptor blockers. In animals that have ingested EtOH chronically, the maintenance of alcohol intake is no longer influenced by EtOH metabolites, as intake is taken over by other brain systems. However, after EtOH withdrawal brain acetaldehyde has a major role in promoting binge-like drinking in the condition known as the "alcohol deprivation effect" a condition seen in animals that have ingested alcohol chronically, are deprived of EtOH for extended periods, and are allowed EtOH re-access. The review also analyzes the behavioral effects of acetate, a metabolite that enters the brain and is responsible for motor incoordination at low doses of EtOH. Also discussed are the paradoxical effects of systemic acetaldehyde. Overall, evidence strongly suggests that brain-generated EtOH metabolites play a major role in the early ("first-hit") development of alcohol reinforcement and in the generation of relapse-like drinking. ©

2015 by the Research Society on Alcoholism.

Acetaldehyde

Acetate

Alcohol deprivation effect

Reinforcement

Salsolinol

Self-administration

acetaldehyde

acetic acid

alcohol

mu opiate receptor antagonist

salsolinol

acetaldehyde

acetic acid derivative

alcohol

isoquinoline derivative

salsolinol

alcohol blood level

alcohol consumption

alcohol metabolism

animal behavior

binge drinking

blood brain barrier

brain metabolism

cerebrospinal fluid

motor coordination

nonhuman

priority journal

Review

animal

brain

drug effects

drug seeking behavior

drug self administration

metabolism

reinforcement

Animalia

Acetaldehyde

Acetates

Animals

Brain

Drug-Seeking Behavior

Ethanol

Isoquinolines

Reinforcement (Psychology)

Self Administration