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FEATURE REVIEW

Genetic polymorphism in ethanol metabolism: acetaldehyde contribution to alcohol abuse and alcoholism

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Acetaldehyde, the first product of ethanol metabolism, has been speculated to be involved in many pharmacological and behavioral effects of ethanol. In particular, acetaldehyde has been suggested to contribute to alcohol abuse and alcoholism. In the present paper, we review current data on the role of acetaldehyde and ethanol metabolism in alcohol consumption and abuse. Ethanol metabolism involves several enzymes. Whereas alcohol dehydrogenase metabolizes the bulk of ethanol within the liver, other enzymes, such as cytochrome *P*4502E1 and catalase, also contributes to the production of acetaldehyde from ethanol oxidation. In turn, acetaldehyde is metabolized by the enzyme aldehyde dehydrogenase. In animal studies, acetaldehyde is mainly reinforcing particularly when injected directly into the brain. In humans, genetic polymorphisms of the enzymes alcohol dehydrogenase and aldehyde

hol drinking habits and the incidence of alcohol

it has been concluded that blood acetaldehyde

In the past decades, it has been speculated that many, if not all of the pharmacological and behavioral effects of ethanol should be attributed to its first metabolite, acetaldehyde. It was even suggested that alcoholism should be renamed 'acetaldehydism'.[5–7]

also be dependent upon its peak blood concen

trations being reinforcing.
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Rewarding properties of acetaldehyde in animal studies

It is generally assumed that the primary factor that controls the propensity to consume ethanol is its positive reinforcing properties.[58] In the last decades, a number of authors have suggested that acetaldehyde contributes to or even mediates the reinforcing effects of ethanol. In animal studies, three lines of evidence argue in favor of this hypothesis. First, there is

are still unclear. Whereas a number of ethanol's

experiment.[64] This study has shown that acetaldehyde is a 1000-fold more potent reinforcer than ethanol when tested for self-administration into the ventral tegmental area, a brain region strongly involved in ethanol reinforcing effects. In addition,

lism, is a biologically active molecule. Aside from its well described hepatotoxic effects,[2] acetaldehyde also

activity generally consume more ethanol. Since catalase is involved in acetaldehyde production within the brain, these studies have concluded that acetaldehyde significantly contributes to the reinforcing effects of ethanol. With a reduced catalase

scientists in the field of alcohol research. Whereas

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ethanol. Pharmacological inhibition of catalase has been shown to reduce ethanol consumption,[73,74] in agreement with the idea that the reinforcing properties of brain acetaldehyde contribute to the motivation to drink alcohol. However, the enzyme catalase is also

localization of its accumulation. In the brain, acetaldehyde induces strong reinforcing effects as demonstrated by a number of studies.[60,61,64,66] In contrast, its

ethanol's effects, others have suggested that alcoholism is in fact a syndrome of 'acetaldehydism'.[5–7]

of its accumulation. While a peripheral accumulation induces a range of unpleasant symptoms that prevent further alcohol drinking, the reinforcing action of brain acetaldehyde is believed to promote alcohol consumption. According to this theory, the overall

we examine recent animal and human studies reporting evidence that acetaldehyde is involved in the pharmacological and behavioral effects of ethanol. The role of acetaldehyde in alcohol abuse and alcoholism will be critically considered with a

In conclusion, there is substantial evidence that acetaldehyde at least contributes to the reinforcing effects of ethanol and is therefore involved in alcohol consumption and abuse.

requirement is fully satisfied.

Ethanol metabolism: an update

In humans, more than 90% of ingested alcohol is eliminated via metabolic degradation mainly in the liver. Ethanol is first metabolized into acetaldehyde through several enzymatic and nonenzymatic