

Involvement of Acetaldehyde in Alcohol Addiction

William J. McBride, Ting-Kai Li, Richard A. Deitrich, Sergey Zimatkin, Brian R. Smith, and Zachary A. Rodd-Henricks

This article presents the proceedings of a symposium at the 2001 RSA Meeting in Montreal, Canada. The organizers and chairs were William J. McBride and Ting-Kai Li. The presentations were (1) Metabolism of ethanol in the brain and the behavioral consequences, by Richard A. Deitrich and Sergey Zimatkin; (2) Catalase production of acetaldehyde as a possible mediator of the psychopharmacological effects of ethanol, by Brian R. Smith; (3) The reinforcing actions of acetaldehyde in the ventral tegmental area, by Zachary A. Rodd-Henricks; and (4) Salsolinol and alcohol addiction, by William J. McBride.

Key Words: Acetaldehyde, Alcohol Addiction, Catalase, Salsolinol.

ACETALDEHYDE (ACD), THE first metabolite of ethanol, is a biologically active compound, and its role in alcohol addiction has been controversial (Hunt, 1996). Peripherally, ACD appears to produce mainly aversive effects. However, there are reports from the human literature that ACD, at low concentrations, also can produce euphoria (Behar et al., 1983). If ACD indeed contributes to the addictive properties of alcohol, several possibilities could

The role of ACD in the actions of ethanol has been a controversial topic for several decades. Drawing on data collected from our laboratory over this period, we contend that the reinforcing properties of ethanol are mediated, at least in part, through the actions of ACD. As well, we self or augments the actions of ethanol. The actions of ACD (or salsolinol) could occur at the membrane level (Smith et al., 1984). However, the observation that the propensity of rats to self-administer ACD was related to their propensity to drink ethanol solutions was the first indication that ACD may play a mediational role in voluntary ethanol consumption (Brown et al., 1980). Further (1991), it is important to establish that ACD can be formed within the brain from physiologically relevant concentra-

Overall, the ICSA data suggest that ACD can produce reinforcing effects within the posterior VTA of P rats and that ACD is a more potent (1000-fold) reinforcer in this region than is ethanol. Additionally, the concentrations of

Zimatkin. The majority of evidence to date supports a role of ACD in producing acute aversive effects and chronic neurotoxic actions. However, there are some reports that ACD may reinforce and mediate the rewarding effects attributed to alcohol. Dr. B. Smith reviewed evidence supporting a role for ACD in mediating the psychopharmacological effects of alcohol and the involvement of catalase as

way. Moreover, significant formation of ACD occurs in vitro in brain tissue at concentrations of ethanol that can be achieved by voluntary consumption of alcohol by the alcohol-preferring P line of rats. Dr. Smith presented data to demonstrate that ACD can produce reinforcing effects and that inhibition of catalase activity prevents many of the behavioral actions of ethanol. These results suggest that many of the behavioral pharmacological effects attributed to ethanol may be a result of the formation of ACD via a catalase reaction. Dr. Rodd-Henricks presented findings that the P rat will self-administer ACD directly into the posterior VTA and that these effects are seen at ACD concentrations that are pharmacologically relevant and can be obtained in brain tissue. These results support the idea that ACD itself can produce reinforcing effects within the limbic system, and they support the involvement of ACD in alcohol addiction. Dr. McBride presented data indicating

perfusion of the brain to remove red blood cells or by use of desferroxamine as a powerful chelator of iron, or both, it has been possible to consistently demonstrate the accumu-

ethanol-naïve NP rats. Overall, the results of this symposium support previous hypotheses concerning a role for ACD and SAL in alcohol addiction. In some cases, ACD by itself may mediate some of the actions of alcohol, whereas in other cases, ACD may promote the actions of alcohol. On the basis of the findings to date, it is not clear what role ACD has in mediating the CNS actions of alcohol. We hope these results will encourage researchers to undertake additional studies with the latest technology to further explore the involvement of ACD in alcohol addiction.

only about 50% or less of the total accumulation of ACD

From Indiana University School of Medicine (WJM, T-KL, ZAR-H), Indianapolis, Indiana; University of Colorado School of Medicine (RAD), Denver, Colorado; Grodno State Medical University (SZ), Grodno, Belarus; and Concordia University (BRS), Montreal, Quebec, Canada.

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Reprint requests: William J. McBride, PhD, Institute of Psychiatric Research, 791 Union Dr., Indianapolis, IN 46202-4887; Fax: 317-274-1365; E-mail: wmcbride@iupui.edu

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