

The Role of Acetaldehyde in the Central Effects of Ethanol

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This article represents the proceedings of a symposium at the 2004 annual meeting of the Research Society on Alcoholism in Vancouver, Canada. The symposium was organized by Etienne Quertemont and chaired by Kathleen A. Grant. The presentations were (1) Behavioral stimulant effects of intracranial injections of ethanol and acetaldehyde in rats, by Mercè Correa, Maria N. Arizzi and John D. Salamone; (2) Behavioral characterization of acetaldehyde in mice, by Etienne Quertemont and Sophie Tambour; (3) Role of brain catalase and central formed acetaldehyde in ethanol's behavioral effects, by Carlos M.G. Aragon; (4) Contrasting the reinforcing actions of acetaldehyde and ethanol within the ventral tegmental area (VTA) of alcohol-preferring (P) rats, by William J. McBride, Zachary A. Rodd, Avram Goldstein, Alejandro Zaffaroni and Ting-Kai Li; and (5) Acetaldehyde increases dopaminergic transmission in the limbic system, by Milena Pisano and Marco Diana.

Key Words: Acetaldehyde, Ethanol, Brain, Catalase, Self-administration, Dopamine.

ACETALDEHYDE, THE FIRST product of ethanol metabolism, is a biologically active compound. As such, it is speculated to play a significant role in alcohol abuse and alcoholism (Quertemont, 2004). However, the

Considerable evidence indicates that acetaldehyde is an active metabolite that contributes to the motor effects of ethanol.

Evidence from several studies suggest that some of the psychopharmacological effects classically attributed to ethanol administration are mediated by its primary metabolite, acetaldehyde (Hunt, 1996; Smith et al., 1997). Acetalde-

Acetaldehyde could contribute to the reinforcing actions of ethanol in several ways.

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peripherally (Quertemont and De Witte, 2001). All these studies lend support to the hypothesis that central actions of ethanol might be mediated by its metabolite acetaldehyde instead.

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In conclusion, the major findings of this study suggest that ethanol and acetaldehyde can produce independent reinforcing effects within the posterior VTA of P rats. However, acetaldehyde is a 1000-fold more potent reinforcer than ethanol in this subregion.

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of animal studies have challenged this common view and suggested instead that acetaldehyde might be reinforcing. Indeed, laboratory rats self-administer acetaldehyde directly into the brain (Rodd-Henricks et al., 2002) as well as

In conclusion the present results suggest that ethanol stimulates dopaminergic transmission in the limbic system through its by-product acetaldehyde, previously thought only as an aversive compound useful in the pharmacological treatment of alcoholics.

brain catalase activity alter the behavioral effects of ethanol particular into the substantia nigra pars reticula. Acetaldehyde was also shown to induce strong amnesic effects at doses below its sedative threshold. Additionally, this ethanol's metabolite was self-administered by rats into the posterior VTA, thereby indicating its reinforcing properties. McBride et al. also showed that acetaldehyde self-infusion requires the activation of dopamine neurons. This conclusive role in ethanol's effects, it is expected to induce

the firing rate of the VTA dopamine neurons. Altogether the results presented here indicated that acetaldehyde exhibits many of the properties that are usually expressed by addictive drugs, i.e., locomotor stimulation, self-administration and activation of dopamine neurons, and therefore suggested that acetaldehyde may play a significant role in alcohol addiction.

BEHAVIORAL STIMULANT EFFECTS OF INTRACRANIAL INJECTIONS OF ETHANOL AND ACETALDEHYDE IN RATS

These results may also bear important consequences on the therapeutic side of alcoholism and drug addiction, in general.

orthless, as is the case with many sedative or depressant

