ETHANOL INDUCED DOPAMINE RELEASE IN THE RAT MESOLIMBIC SYSTEM. ROLE OF ACETHALDEHYDE

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Acethaldehyde (ACD) is the first metabolite of ethanol (EtOH), produced primarily by alcohol dehydrogenase (ADH) and cytochrome P450 in the periphery, and by catalase in the central nervous system (1).
Once considered just an aversive metabolite, ACD is now recognised as a bioactive compound possibly implicated in many of the behavioural, toxic, and psycostimulant effects of ethanol (1). Recent evidence support the hypothesis that ACD mediates some of the reinforcing effects of EtOH. In fact, ACD induces a positive place conditioning after intracerebro-ventricular or intra-peritoneal (i.p.) administration, is self-administrated in the VTA by laboratory rats (2) and recent *in vivo* electrophysiological data show that EtOH-induced stimulation of VTA DAergic neurones is prevented by the administration of the AHD competitive inhibitor 4-metylpyrazole (4MP) (3). Interestingly, administration of the ACD inactivating agent D-penicillamine (Dpnc) prevents ethanol induced behavioral stimulation and decreases voluntary ethanol consumption in laboratory rats (4). In this study, in view of the key role of the mesolimbic dopamine (DA) system in the neurobiological basis of the reinforcing effects of ethanol, we used *in vivo* microdialysis to evaluate extracellular DA levels in the *Nucleus Accumbens* (Nacb) shell after a challenge with ACD and EtOH both in control and in Dpnc- and 4MP-pretreated rats.
Materials and method. Male albino Wistar (280-300g) were implanted with an I-shape dialysis probe aimed at the NAcb shell. DA extracellular levels were monitored after administration by gavage (i.g.) of ACD (10, 20, 40mg/kg) or EtOH (0.5, 1, 2 g/kg). Animal pretreatment with 4MP (45mg/kg i.p.) or Dpnc (50mg/kg i.p.), occurred respectively 24 hours and one hour before EtOH or ACD i.g. administration.
Results. In our hands, both ACD and EtOH were able to increase DA extracellular concentration in the NAcb shell (up to 50% and 35% from basaline levels, respectively), while no effects were observed after EtOH or ACD administration in the rats pre-treated with D-penicillamine. In animal pretreated with 4MP, administration of EtOH did not elicit any increase in Nacb DA levels.
Conclusions. The present data show that ACD by itself and derived from ingested ethanol, do promotes DA release in the NAcb shell. These findings are consistent with the hypothesis that ACD directly stimulates DA neurons projecting to the NAcb. Therefore, in this circumstance ethanol may function as a pro-drug being able to stimulate the activity of the mesolimbic DA system, via its main metabolite ACD.

References:

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