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Possible Role of Brain Biogenic Amines in the Disulfiram-Ethanol Reaction

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The "disulfiram-ethanol reaction" (DER) refers to the unpleasant symptoms experienced upon drinking alcoholic beverages after having previously ingested disulfiram. The possible underlying mechanism is the increase of blood acetaldehyde due to inhibition of the liver aldehyde dehydrogenase. According to clinical reports, several other medicinal products can also cause this reaction. In order to investigate the mechanism of this manifestation the following substances were administered intraperitoneally to Wistar rats: disulfiram (100 mg/kg b.w), chlorpropamide (80 mg/kg b.w), procarbazine (100 mg/kg b.w), furazolidone (100 mg/kg b.w), griseofulvin (100 mg/kg b.w) and isoniazid (100 mg/kg b.w). We measured the hepatic enzyme activities of alcohol and aldehyde dehydrogenases (ADH, ALDH) as well as the cytochrome P450 isozyme CYP2E1. Additionally, in four structures of the brain (striatum, hypothalamus, midbrain and frontal cortex) the level of noradrenaline (NA), dopamine (DA), dixydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) were determined by HPLC with an electrochemical detector. All substances tested inhibited the low-Km ALDH, with the exception of griseofulvin; the high-Km ALDH responded in an inconsistent way. CYP2E1 was inhibited by disulfiram and chlorpropamide while it was induced by isoniazid; ADH was not affected at all. Concerning the level of brain biogenic amines, remarkable differences were observed between control and experimental animals. Our results suggest that the DER is mediated mainly, but not exclusively, by inhibition of the low-Km ALDH. Additionally, alterations on brain biogenic amines may play an important role in the mediation of this reaction.