Influence of Ethanol on the Acetyl-Coenzyme A Level of Intact Rat Liver

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The bulk of the consumed ethanol is oxidized in the liver to acetate.[1] The concentration of this metabolite in the body increases consequently. The formation of fatty acids [2] and ketone bodies [3] is not notably influenced. When acetate without ethanol is used as substrate for the liver, it is readily oxidized to carbon dioxide, incorporated into fatty acids [4] and, to a smaller content, into ketone bodies.[5] Acetyl-CoA is a common metabolite in all these reactions and the concentration of this compound in the liver was, therefore, studied during ethanol metabolism.

An analysis was made of the acetyl-CoA content of livers of albino rats from our own laboratory stock, weighing 200–300 g and fed a normal diet. 1.6 g of ethanol per kg body weight was administered as a 10 % solution to one group of rats by stomach tube one hour before liver excision. Samples of the livers were taken after nembutal anaesthesia by application of the freeze-stop technique.[6] Elution of the protein-free fraction containing the acetyl-CoA from the frozen liver and spectrophotometric determination of the acetyl-CoA by means of the malate-coupled assay were performed in the same way as used by Wieland and Weiss.[7] The results have not been corrected although it has been demonstrated that the method gives values which are somewhat too low.[8,9]

The acetyl-CoA levels of the control rats and of the ethanol-loaded rats are presented in Table 1. There was a 50 % increase in the acetyl-CoA concentration in the ethanol-loaded animals, and the difference was highly significant ($p < 0.005$). A pronounced difference also existed in the susceptibility of male and female rats to the effect of ethanol. Ethanol produced a 34 % increase in the acetyl-CoA level of the liver of male rats, but in female rats this increase amounted to 80 %.

Table 1. Acetyl-CoA levels of livers from control rats and rats administered ethanol. Liver samples taken by the freeze-stop technique. Mean values ± s.d. are given, with the number of experiments in parenthesis.

	Control	Ethanol	Increase
	mμmoles acetyl-CoA/g fresh liver		%
Males	22.1±7.1 (9)	29.6± 6.3 (9)	34.2
Females	18.2±5.1 (6)	32.7±12.6 (6)	79.9
Males + females	20.5±6.4 (15)	30.8± 9.0 (15)	50.3

The increased acetyl-CoA level reported here can be explained either as a result of activation of acetate derived from ethanol or as an impaired end-oxidation of fatty acids. Ammon *et al.*[10] have shown that the concentration of active CoA of the liver decreases strongly, and a slightly decreased acyl-CoA level is also reported during ethanol metabolism.[11] The accumulation of acetyl-CoA is probably mostly intramitochondrial, resulting from an impaired inflow in the citric acid cycle, and this depresses, consequently, the extramitochondrial formation of fatty acids from cleaved citrate. The formation of ketone bodies is not reported to increase during ethanol oxidation and this is surprising, since it has been assumed that the elevated acetyl-CoA level found in diabetes and after feeding fat [7] is the primary ketogenic cause in these two situations.

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