Reduction of Alcohol Dependence in Rats after Carotid Glomectomy

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Carotid glomectomy significantly reduced the degree of alcohol addiction in rats, which was induced over 12 weeks. After glomectomy, the mean weekly volume of alcohol consumed by alcoholic animals over 4 weeks was lower compared to the preoperation level, while water consumption significantly increased by the 3rd and 4th weeks after surgery. Control sham operation had no effect on ethanol and water consumption in alcoholic rats. Possible involvement of the local renin-angiotensin system in chemoreceptor cells of the carotid body into systemic mechanisms of alcohol dependence is discussed.

Key words: *alcohol dependence; ethanol; carotid body; renin-angiotensin system*

The development of alcohol dependence and its consequences is associated with changes in the modality of motivational excitements in the brain and variations in the hormonal regulation of functions, hemodynamic parameters, and water-salt balance in the organism. Apart from cholinergic influences, the renin-angiotensin system (RAS) plays a role in the maintenance of thirst and thirst-based alcohol addiction. Significant changes in RAS of rats after chronic alcohol consumption are followed by impairment of drinking behavior [3,4,10,11,14]. Little is known about the role of peripheral RAS structures (*e.g.*, receptors on blood vessels) in the mechanisms of thirst and associated alcohol motivation. Cells of the carotid body (CB) express RAS components. Afferent signals from the chemoreceptor apparatus of CB are observed not only in response to variations in the concentration of oxygen and carbon dioxide and osmotic blood pressure, but also in the presence of angiotensin II [1,5, 8,9,12,13,15]. Systemic administration of angiotensin II did not induce thirst and "salt appetite" in rats after bilateral excision of CB (carotid glomectomy, CGLE). Intracerebroventricular injection of angiotensin II to these rats was followed by increased consumption of water and sodium chloride [6,7]. We hypothesized that CB with local RAS plays a role not only in the regulation of water and saline consumption, but also in the development and realization of alcohol dependence formed on the structural and functional basis of thirst motivation.

Here we studied the development and realization of alcohol addiction in rats after CGLE.

MATERIALS AND METHODS

Experiments were performed on 39 Wistar rats weighing 230-250 g. The animals were housed in individual cages and had free access to standard pelleted feed. The effect of CGLE on alcohol addiction in rats was studied in 2 series. In series I, CGLE was performed in 9 animals of the treatment group. Control animals (n=9) were sham-operated under ether anesthesia [2]. The animals were given a burette with 15% aqueous solution of ethanol as the

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sole source of fluid for 12 weeks. After forced alcoholization, the rats received 15% ethanol and water *ad libitum* for 4 weeks. In series II, 21 intact rats were alcoholized with 15% ethanol for 12 weeks. Then they received 15% ethanol and water *ad libitum* for 2 weeks. CGLE was performed in 12 rats of the treatment group. Control animals (n=9) were sham-operated. Ethanol and water were given over 4 weeks after surgery. Daily volumes of consumed alcohol and water (ml) were measured for each alcoholic rat during the preoperation and postoperation periods and standardized per 100 g body weight. We calculated total weekly volume of alcohol and water for each rat and mean weekly volume of fluids for the group of sham-operated and CGLE animals. In series I, we compared weekly volumes of water and alcohol consumption in treated and control animals. In series II, we compared the volumes of fluids consumed over each week after surgery. These parameters were compared with the volume of fluid consumed over the 1st week before surgery (100% in treated and control animals).

The results were analyzed by Wilcoxon test.

RESULTS

Series I showed that CGLE had no effect on the development of alcohol dependence in rats. The weekly volume of ethanol and water consumed by CGLE animals after alcoholization reflected the development of alcohol dependence (daily consumption of 0.8-2.5 ml/100 g ethanol for 4 weeks) and did not differ from that in sham-operated rats.

Series II showed that CGLE in rats was followed by reduction of pre-developed alcohol addiction (*i.e.*, realization of alcohol motivation). Studying the consumption of alcohol and water by intact rats over the 1st and 2nd weeks before surgery revealed the development of alcohol addiction due to alcoholization. The volumes of fluids consumed by these animals did not differ over the first 2 weeks before surgery. Alcohol consumption over 4 weeks after CGLE was lower compared to that during the 1st week before surgery. The mean volume of alcohol consumption decreased by 56.6% over the 1st week after surgery (Fig. 1, *a*). The mean volume of water consumption significantly increased by the 3rd and 4th week after surgery compared to the preoperation level (Fig. 1, *b*). Sham operation had no effect on the consumption of ethanol and water in alcoholic rats (Fig. 1).

Thirst, as well as alcohol motivation on the structural and functional basis of thirst, may be regulated by general and specific mechanisms. The volume of ethanol consumed by rats sharply decreased over the 1st and 2nd weeks after CGLE. The volume of water consumption remained unchanged during this period, but significantly increased by the 3rd and 4th weeks (Fig. 1). Rapid decrease in ethanol consumption over the 1st week after CGLE probably reflects an important role of the center-peripheral interactions in this process. Chronic alcohol consumption is followed by dysfunction of cerebral and periphery structures of RAS and development of alcohol addiction [3,4,11,14]. After CGLE, central structures do not receive afferent signals from angiotensin II-sensitive chemoreceptors and CB osmoreceptors. These receptors play an important role in the regulation of fluid consumption, which depends on activity of RAS. The deficiency of carotid regulation can be followed by compensatory functional reorganization of central

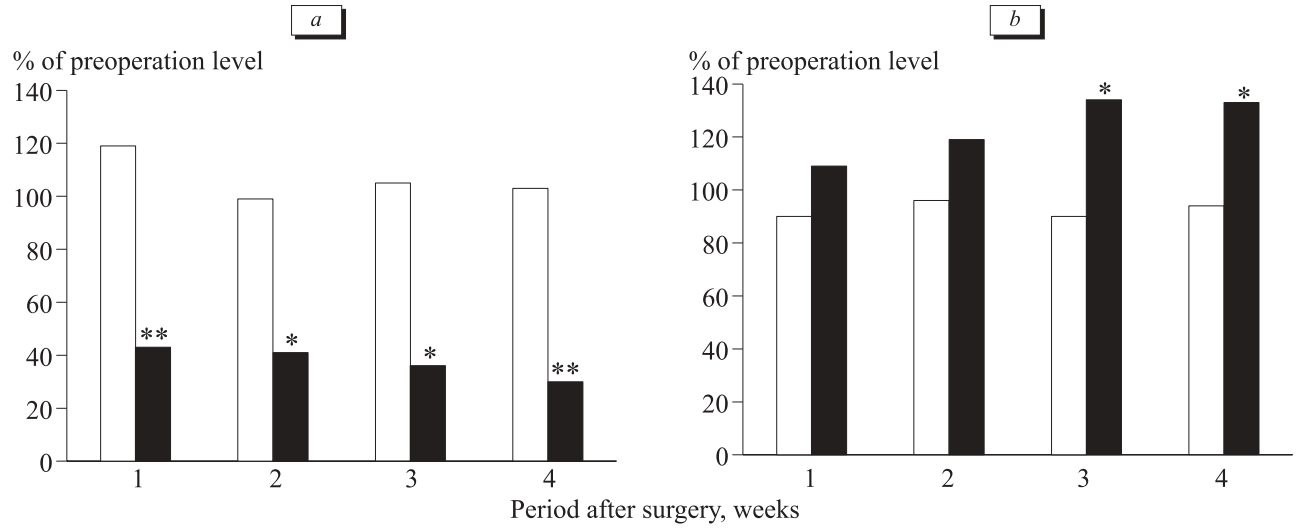

Fig. 1. Consumption of alcohol (*a*) and water (*b*) in rats with alcohol dependence after CGLE. Light bars, sham-operated rats; dark bars, CGLE rats. *p<0.05 and **p<0.01 compared to the preoperation level.

RAS structures in alcoholic animals. This process is directed toward the reduction of alcohol motivation and increase in thirst.

Our results show that CB not playing a role in the development of alcohol addiction, regulates the realization of alcohol motivation.

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