CHANGES IN PITUITARY CONADOTROPHIC FUNCTION DURING DEVELOPMENT OF EXPERIMENTAL ALCOHOLISM IN RATS

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UDC 616.89-008.441.13-092.9-06:
616.832-008.6:577.175.327

KEY WORDS: experimental alcoholism; pituitary; luteinizing hormone; prolactin.

Ethanol causes morphological and functional changes in the gonads of animals and man [2]. However, the locus of the lesion in the pituitary-gonadal system is not yet known. Most investigators are inclined to regard the antigonadal effect of ethanol as the result of its direct toxic action on testicular steroidogenesis [6]. Meanwhile there are indications of a change in the secretion of gonadal releasing hormones, especially following acute administration of ethanol [7]. Nevertheless, the dynamics of gonadotrophin secretion in the period of formation and development of alcoholism has not yet been studied.

In the present invstigation on a model of experimental alcoholism, distinguishing the stages of its development, secretion of prolactin and luteinizing hormone (LH) was studied.

METHODS

Experiments were carried out on male albino rats of a mixed population weighing 250-380 g, kept on a pellet diet. According to the experimental model of alcoholism [4], motivation for alcohol (the 1st stage) and a state of physical dependence on ethanol (3rd stage) were formed in the rats after contact with ethanol for 10 days and 8 months respectively. The animals were given free choice between water and 15% ethanol. Consumption of water and 15% ethanol was recorded on alternate days by measuring the change in the level of the liquid in burettes. Animals consuming not less than 60 ml of 15% ethanol were considered to be heavy drinkers, whereas animals whose mean daily consumption of 15% ethanol did not exceed 6 ml/kg body weight were regarded as abstemious. The animals took part in the experiment directly from cages equipped with drinking bowls containing water and ethanol, and were decapitated between 11 a.m. and noon. Blood was collected in test tubes containing EDTA (final concentration 1 mg/ml) and the plasma was separated. The pituitary glands of the rats (without the posterior lobe) were homogenized in physiological saline (final concentration 1 mg/ml). Hormone concentrations were determined by means of specific antisera obtained in the Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, by methods described previously [1, 3].

RESULTS

It will be clear from Table 1 that the LH levels in the blood plasma and pituitary gland of rats differing in their ethanol consumption (abstemious and heavy drinkers) after contact with ethanol for 10 days were identical, and corresponded to values characteristic of pooled blood plasma from intact animals (32.05 ng/ml).

In the 3rd stage of experimental alcoholism the LH levels in the plasma and pituitary gland of the abstemious and heavy-drinking rats also were identical. Meanwhile, data obtained previously in the Institute of Pharmacology, Academy of Medical Sciences of the USSR, are evidence of a sharp fall in the total concentration of testosterone and 5α-dihydrotestosterone at the stage of formation of motivation for alcohol in both heavy-drinking and

Department of Neuropharmacology, Institute of Pharmacology, Academy of Medical Sciences of the USSR. Laboratory of Physiology of the Endocrine Systen and Laboratory of Biological Testing of Hormones, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Val'dman.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 101, No. 6, pp. 675-676, June, 1986. Original article submitted December 14, 1984.

TABLE 1. Gonadotrophin Levels in Rats during Development of Experimental Alcoholism (M ± m)

Stage of experimental alcoholism	Animals	Plasma prolactin, ng/ml		LH		
				Plasma, ng/ml		Pituitary, µg/mg tissue
1st	Heavy drinkers (8)	15,9±1,53	(4)	38,6±6,3	(4)	4,5±0,08
	Abstemious (7)	19,36±1,54	(4)	43,7±14,9	(4)	4,4±0,20
3rd	Heavy drinkers (8)	29,8±8,77	(5)	27,05±3,0	(4)	3,7±0,46
	Abstemious (7)	9,8±1,3*	(5)	28,0±2,98	(4)	4,0±0,52

Legend. Number of animals given in parentheses. *P < 0.05 compared with heavy drinking rats (3rd stage).

abstemious rats. The androgen level remained considerably depressed also in the 3rd stage of experimental alcoholism in the heavy-drinking animals [5]. Consequently, in the course of development of experimental alcoholism the LH level remained unchanged and adequate release of gonadotropins in response to a sharp decline in the steroid-synthesizing function of the gonads was not observed. This points to uncoupling of the feedback mechanisms between the gonads and the pituitary. Disassociation of this kind may be due, on the one hand, to a change in the sensitivity of steroid-sensitive neurons in the mediobasal hypothalamus to the action of testosterone, and on the other hand, to a disturbance of the response of pituitary gonadotrophins to LH releasing hormone.

Prolactin secretion, which has a negative effect on testosterone synthesis, was identical in abstemious and heavy-drinking animals after contact with ethanol for 10 days, but its level was a little higher than that of the hormone in pooled material from intact rats (9.68 ng/ml). In the 3rd stage of experimental alcoholsim a raised hormone level was still found only in the heavy-drinking rats. Hyperprolactinemia is known to be highly characteristic of clinical alcoholism, and the fall of the testosterone level and the increase in the concentration of estrogens circulating in the blood stream is connected with it [8].

Thus the clear negative correlation between the high prolactin level and the low testosterone concentration in animals of the different groups during the development of experimental alcoholism suggests that hypersecretion of prolactin is one cause of the depression of testicular steroidogenesis. Meanwhile, inadequate secretion of LH is another factor maintaining this process. Correspndingly, there are grounds for considering that hypogonadism observed during the development of experimental alcoholism is due not only to the toxic action of ethanol on the steroid-synthesizing cells of the testis, but also to a change in secretion of LH and prolactin.

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