The results of the present investigation, showing that opioid peptides can inhibit gastric acid secretion confirm the writer's previous findings of analogous effects following administration of leucine- and methionine-enkephalins [1, 2], and they also agree with the result of experiments on dogs when initial stimulation of secretion was induced by food [4].

Meanwhile the present investigation confirmed once again our hypothesis on the physiological inhibitory activity of peptides in small doses only, which was demonstrated in the case of casomorphine, when an increase in the dose of the compound to 100 μg/kg/h significantly reduced the inhibition of HCl secretion. A similar effect was observed by the writers previously when testing activity of methionine-enkephalin [2]. Furthermore, this result may explain the possibility of stimulation of gastric secretion by the use of opioid peptides in increasing doses [5].

Opioid peptides of both endogenous and exogenous origin thus have a considerable inhibitory action on gastric secretion, and this is further confirmation of the importance of the study of their role in the regulation of gastric secretory processes.

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CHARACTERISTICS OF THE ENDOCRINE SYSTEM OF RATS DIFFERING IN INCLINATION FOR VOLUNTARY ETHANOL CONSUMPTION

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Administration of a single and repeated doses of ethanol causes marked and varied changes in the function of several endocrine organs both in man and in experimental animals [3-6]. On this basis an endocrine nature of certain etiologic and pathogenetic factors of alcoholism has been postulated [7, 9]. However, when standard models of experimental alcoholism are used it is impossible to differentiate between primary etiologic endocrinopathies and secondary hormonal disturbances caused by ethanol administration.

The possibility of selecting animals with a constitutional inclination for voluntary ethanol consumption from the general population of noninbred rats goes some way toward solving the problem of whether endocrine disturbances are the result of development of alcoholism or whether individual variability in hormonal status can be regarded as one of the primary factors provoking the development of this disease. Accordingly animals predisposed and not predisposed to voluntary consumption of ethanol were used as models with which to study the function of

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TABLE 1. Hormone Concentrations in Blood Plasma of Rats with Different Levels of Alcohol Motivation

Hormone	Number of rats	Predisposed animals	Number of rats	Animals not predisposed
ACTH, ng/ml	8	7,88±1,58 $P<0,001$	6	2,58±0,69
β-endorphin, fmoles/ml	6	207,1±25,9 $P<0,01$	6	82,1±16,3
LH, ng/ml	5	30,03±2,95 $P>0,05$	6	34,7±2,83
Testosterone + 5α-dihydrotestosterone, ng/ml	5	5,50±0,98 $P>0,05$	5	5,35±0,24
17β-estradiol, pg/ml	6	83,5±1,35 $P>0,05$	6	92,95±5,5

the pituitary-gonadal and pituitary-adrenal systems — the most vulnerable components of the hormonal sphere in the development of alcoholism.

EXPERIMENTAL METHOD

Experiments were carried out on male noninbred albino rats weighing 200-250 g, kept on pellet diet. To separate rats predisposed and not predisposed to ethanol consumption, the criterion of the duration of ethanol narcosis was used [2], namely the time spent by the rats in the side position after intraperitoneal injection of 25% ethanol in a dose of 4.75 g/kg. Rats sleeping for a short time (mean 30-40 min) were regarded as being predisposed, rats sleeping for a long time (over 100 min) were considered not predisposed to voluntary consumption of ethanol. The animals were decapitated (not later than 11 a.m., 10-14 days after injection of a test dose of ethanol). To determine steroid hormones, plasma was separated from blood containing heparin (10 Units/ml). To determine pituitary hormones, the sodium salt of EDTA was added (1 mg/ml) to the blood.

The pituitary glands of the rats was homogenized in physiological saline (final concentration 1 mg/ml). The content of all hormones was determined radioimmunologically by means of commercial kits: testosterone + 5α-dihydrotestosterone (Amersham, England), 17β-estradiol and ACTH (Sorin, France), and β-endorphin (New England Nuclear, USA). The leuteinizing hormone (LH) levels were studied at the Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, by means of an antiserum obtained in the laboratory of Physiology of the Endocrine System [1]. The numerical results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Although a lesion of the pituitary-gonadal axis is the most characteristic endocrinopathy in experimental and clinical alcoholism, no significant differences in the concentration of 17β-estradiol, the combined concentration of testosterone and 5α-dihydrotestosterone, and also in the LH level could be detected in these experiments in the blood plasma of rats predisposed and not predisposed to voluntary ethanol consumption (Table 1). The combined concentration of testosterone and 5α-dihydrotestoserone in rats predisposed and not predisposed to voluntary ethanol consumption was 5.50 ± 0.98 and 5.35 ± 0.25 ng/ml ($P > 0.05$) and the corresponding figures for 17β-estradiol were 83.50 ± 1.35 and 92.95 ± 5.50 pg/mg ($P > 0.05$). The ratio of estrogens and androgens in the blood, known as the estrogen—androgen index, was 1.15 in rats predisposed to voluntary ethanol consumption, but 1.73 in rats not so predisposed. The corresponding index for intact animals of this age was 1.71. The plasma LH level in rats of the two groups did not differ statistically significantly and was 30.03 ± 2.95 and 34.70 ± 2.83 ng/ml in animals predisposed and not predisposed respectively to ethanol consumption.

To rule out the possibility of loss of coordination in the feedback mechanism between the pituitary and gonads in rats with different levels of alcohol motivation, the LH level was studied in pituitary homogenate of the two groups of rats. The LH concentration in pituitary homogenate from rats predisposed and not predisposed to ethanol consumption did not differ

significantly and was 3662.07 ± 133.0 and 3869.3 ± 94.2 ng/ml tissue respectively ($P > 0.05$). This suggested that pituitary-gonadal function is not disturbed in animals with an increased inclination for voluntary ethanol consumption. Meanwhile the plasma ACTH concentration in rats predisposed to ethanol consumption was more than three times higher than in animals not so predisposed. Moreover, animals inclined toward voluntary ethanol consumption were distinguished by a higher level of β-endorphin immunoreactivity, which is known to accompany increased ACTH secretion in stress states and, in addition, β-endorphin has a precursor with ACTH and a common releasing factor [8].

The results are evidence of increased function of the pituitary-adrenal system, manifested as hyperproduction not only of ACTH, but also of the accompanying hormone. Considering the marked psychopharmacological properties of ACTH and β-endorphin, which play the dual roles of hormones and neurotransmitters, their interaction with central and peripheral opiate receptors, and also the hypothesis that ACTH or its fragments participate in the pathogenesis of dysphoric states in animals and man [9], we regard the raised level of ACTH and β-endorphin as a biochemical indicator of predisposition toward ethanol consumption, on the one hand, and as an important etiological factor for the formation of alcohol motivation, on the other hand.

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