To discover the precise values of these exponents and to work with them, it is convenient to use a semilogarithmic scale, by means of which these exponential curves are converted into straight lines, and for that reason a logarithmic signal amplifier was introduced.

An example of synchronous recording of all three curves (change of volume, rate of change of volume, and logarithm of change of volume) is illustrated in Fig. 2.

The use of this apparatus has proved useful in studies of the peripheral circulation by the VOP method in healthy subjects and also in patients with disturbances of the peripheral circulation.

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ROLE OF SEX HORMONES IN THE MECHANISM OF THE EFFECT OF MONOAMINES ON LH-RH LEVEL IN THE HYPOTHALAMUS

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Evidence has been obtained that monoamines of the CNS take part in the regulation of pituitary gonadotrophic function [3, 7]. The sex hormones play an important role in this situation. However, most research has been devoted to the study of the effect of sex steroids on secretion of luteinizing hormone (LH), and there have been only isolated studies of the changes observed under these circumstances in the content of LH releasing hormone (LH-RH) in the hypothalamus [4, 5].

The aim of the present investigation was to study the effect of monoamines (noradrenalin, serotonin, dopamine) on the LH-RH content in the arcuate nuclei (AN) and median eminence (ME) of the hypothalamus and also in the preoptic region (PO) of intact and castrated male rats. It is in these regions that the bodies of neurons which secrete LH-RH are located. The blood levels of LH-RH and LH were determined at the same time.

EXPERIMENTAL METHOD

Adult male rats were used, and some of them were castrated 2 weeks before the experiment. In a stereotaxic apparatus noradrenalin bitartrate (NA), dopamine (DA), or serotonin creatinine-sulfate (5-HT) in a dose of 10 or 20 μg in 2 or 4 μl, respectively, of physiological saline, was injected into the third ventricle of the animals of the experimental group. Animals of the control group received physiological saline. The animals were killed 15 min later and the brain was removed and cut into sections on a freezing microtome. The structures for testing were removed from sections 300 μ thick by the puncture method [6]. The

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TABLE 1. LH-RH Concentration (in pg/μg protein) in Different Brain Regions and Blood Levels of LH-RH and LH in Rats after Intraventricular Injection of Monoamines (10 μg)

Conditions	Group of animals	PO	AN	ME	Blood	
					LH-RH, pg/ml	LH, ng/ml
Control	Intact	0,21±0,04	3,2±0,3 $P<0,01$	33,5±2,8	25,0±2,3	116,6±13,0
	Castrated	0,28±0,03	1,9±0,1	24,5±2,1	24,5±2,1	254,5±22,1
NA	Intact	0,19±0,05	2,7±0,3	15,9±1,3	44,9±6,3	181,0±13,4
	Castrated	0,15±0,02	2,3±0,3	28,7±4,1	28,0±4,1	250,0±26,1
DA	Intact	0,14±0,01	3,15±0,4	26,5±2,4	34,1±3,0	137,2±10,3
	Castrated	0,18±0,02	2,8±0,2	18,6±1,99	20,0±1,8	235,0±28,0
5-HT	Intact	0,2±0,03	2,8±0,4	23,6±3,2	21,6±2,4	87,0±7,4
	Castrated	0,15±0,03	2,6±0,3	18,7±2,6	20,0±3,2	179,0±19,3

Legend. LH-RH level in ME of intact animals (control — NA), $P < 0.001$. Mean results of seven experiments shown.

TABLE 2. LH-RH Concentration (in pg/μg protein) in Different Brain Regions and Blood LH-RH (in pg/ml) and LH (in ng/ml) Levels in Rats after Intraventricular Injection of Monoamines (20 μg)

Conditions	PO	AN	ME	Blood	
				LH-RH, pg/ml	LH, ng/ml
Intact animals	0,15±0,04	3,3±0,22 $P<0,001$	26,8±0,9 $P<0,05$	52,5±3,9	62,5±8,1 $P<0,001$
Castration + physiological saline	0,26±0,04	2,5±0,23	22,6±1,5	39,6±8,6	138,9±10,7
Castration + NA	0,20±0,05	2,02±0,3	19,8±1,6	55,1±4,9	172,3±15,3
Castration + DA	0,17±0,02	2,8±0,29	22,3±1,5	54,3±3,8	99,3±4,7
Castration + 5-HT	0,22±0,02	2,4±0,29	21,2±2,5	75,6±5,3	84,02±5,3

Legend. LH level in castrated animals (physiological saline — DA) $P < 0.05$. Mean results of six experiments shown.

LH-RH content was determined by a radioimmunologic method [2] in pooled samples from three or four animals [2], and expressed per microgram protein. The blood levels of LH-RH and LH also were determined by a radioimmunologic method [1].

EXPERIMENTAL RESULTS

The LH-RH content in PO 2 weeks after castration was increased, but the level of the hormone in AN and ME was reduced at that time (Table 1). Although the blood level of LH-RH was unchanged under these circumstances, the LH level was more than doubled. It can be postulated that after the sharp fall in the level of sex hormones in the blood as a result of castration, the inhibitory action of sex steroids was abolished, the supply of LH-RH from AN and ME and, hence, into the blood, was increased, with the result that liberation of LH from the pituitary was increased. The absence of any significant changes in the blood LH-RH concentration may be due to the more rapid utilization of this hormone at the cellular level. On the basis of these data showing that the most marked changes in the LH-RH content occurred in ME it can be concluded that this region is the point of application of androgens in the system of the negative feedback mechanism.

Injection of NA in a dose of 10 μg into intact animals raised the blood levels of LH-RH and LH. However, injection of this dose of NA into castrated animals gives only a very small increase in the blood LH-RH concentration compared with the control. The LH concentration in castrated animals receiving NA was increased by the same degree as in control castrated animals (Table 1).

Comparison of the action of NA on intact and castrated animals showed that the LH-RH concentration in PO was reduced by 21.1% and in AN by 15%. The LH-RH level in ME was increased by 46%. Against the background of a sharp fall in the level of sex steroids, NA in

the dose used (10 μg) was thus less effective. There is evidence that if increasing doses of NA are administered a dose-dependent effect on LH secretion is observed. Another series of experiments was accordingly carried out in which the animals were injected with 20 μg NA. Under these conditions (Table 2) the blood level of LH-RH in the castrated animals receiving NA was increased by 39.1% compared with the control, whereas the blood LH concentration was increased by 24.05%.

After injection of 10 μg DA into intact animals (Table 1) no significant differences were found in the LH-RH content in PO and AN compared with the control. The LH-RH content in ME was reduced by 26.5%, but in the blood it was increased by 36.4%. The blood LH level also was increased a little. Judging by the data, DA may perhaps facilitate release of LH-RH from nerve endings in ME to some extent, as a result of which the blood LH level rose.

After injection of the same dose of DA into castrated rats the LH-RH concentration in PO was increased by 30%. The opposite reaction was noted in AN, ME, and in the blood, in which the fall in the LH-RH level amounted to 13.5, 29.8, and 41.4%, respectively. A significant increase in the LH concentration was observed in the blood, but it did not exceed the level of the castrated control. Possibly in this case also the lowered LH-RH content in ME could be evidence of increased liberation of the hormone under the influence of DA from nerve endings in ME. Increasing the dose of DA to 20 μg, unlike NA, did not cause any increase in the blood LH level above its level in castrated control animals.

Injection of 5-HT into intact male rats did not affect the LH-RH concentration in PO. The level of the hormone was lowered in AN and ME. The LH concentration in the blood was reduced by 25.70%. It can be postulated that unlike NA, which lowered the LH-RH level in AN and ME because of activation of release of the hormone from cells of AN and stimulation of liberation of LH-RH from nerve endings in ME, 5-HT inhibits LH-RH synthesis in AN neurons, so that a smaller quantity of the hormone was supplied to ME and the blood stream.

Comparison of parameters of castrated and intact animals after receiving an injection 10 μg 5-HT revealed a marked fall in the LH-RH level in PO and a small fall in AN and ME. The LH-RH concentration in the blood was unchanged. The LH level in the blood was lowered by almost 30% compared with that of the castrated animals of the control group. A higher dose of 5-HT (Table 2) caused further inhibition of LH secretion by the pituitary in the castrated rats. In this case the blood LH-RH level was raised. Here, therefore, an opposite situation arose, with an increase in the blood LH-RH concentration and a fall in the LH level. It can be tentatively suggested that 5-HT has a blocking action directly on the pituitary gonadotrophs, like that which has been demonstrated for DA and the thyrotrophs of the adenohypophysis.

After injection of monoamines into the third ventricle their action may spread around the ventricle to LH-RH neurons, whose bodies lie near the arcuate nuclei. The possibility of axo-axonal connections likewise cannot be ruled out between dopaminergic axons and terminals of LH-RH neurons in ME. The results obtained by injection of monoamines in the present experiments into intact and castrated animals suggest that the intensity and, perhaps, the direction of their action largely depends on the endocrine status of the animals. The effect of monoamines on LH-RH neurons is steroid-dependent.

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