LG obtained by the method described above thus closely resemble, in all characteristics it is possible to compare, LG *in situ* [2, 4, 5, 7, 9, 13-15]. This encourages the hope that the preparations obtained (fractions F_3 and F_4) are actually rich in lipofuscin. The method examined above yields LG in quantities sufficient for their subsequent analysis by physicochemical methods.

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EFFECT OF STEROID AROMATASE INHIBITORS OH HYPOTHALAMIC CATECHOLAMINE CONTENT IN NEONATALLY ANDREGENIZED RATS

N. D. Nosenko and A. G. Reznikov

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KEY WORDS: androgens; aromatase inhibitors; catecholamines; sexual differentiation of the brain

It was shown previously that the defeminizing effect of testostrone on the developing brain of female rats is realized through accumulation of noradrenalin in the hypothalamus [3, 10]. Selective inhibition of catecholamine synthesis by injection of α-methyl-p-tyrosine prevents the development of anovulatory sterility in neonatally adrogenized rats [11]. A similar effect also was obtained by the use of aromatase inhibitors [4], confirming the important role of conversion of androgens into estrogens in androgen-dependent sexual differentiation of the brain (SDB) [8].

The aim of this investigation was to study the ability of aromatase inhibitors to prevent the rise in NA concentration in the hypothalamus induced by injection of exogenous testosterone into newborn female rats.

EXPERIMENTAL METHOD

Experiments were carried out on 140 newborn Wistar rats. Testosterone propionate (TP) was injected subcutaneously in a dose of 50 μg on the 5th day after birth. The aromatase inhibitors 4-androstene-3,6,17-trione (AT), in a dose of 0.5 mg, and 1,4,6-androstatriene-3,17-dione (ATD), in a dose of 1 mg (Steraloids, USA) were injected together with TP on the 5th day

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TABLE 1. Concentrations of Noradrenalin and Dopamine (nmoles/g tissue) in Hypothalamus of Neonatally Andregenized Rats on 7th-12th Day after Birth (M ± m)

Age, days	Group of animals	Number of animals	NA	Dopamine
7	Oil	15	2,66±0,41 (5)	1,66±0,35 (5)
	TP	18	3,06±0,29 (5)	1,74±0,15 (5)
8	Oil	10	2,96±0,29 (5)	1,72±0,21 (5)
	TP	11	3,56±0,44 (5)	1,74±0,35 (5)
10	Oil	12	3,34±0,33 (5)	2,82±0,49 (5)
	TP	13	4,54±0,38* (5)	4,72±0,27** (5)
12	Oil	8	4,10±0,39 (4)	3,48±0,49 (4)
	TP	8	3,40±0,58 (3)	2,53±0,64 (3)

Legend. Here and in Table 2, *p < 0.05, **p < 0.01, ***p < 0.001 compared with control. Number of analyses given in parentheses.

TABLE 2. Concentrations of Noradrenalin and Dopamine (nmoles/g tissue) in Hypothalamus of 10-day-old Rats after Injection of TP and Aromatase Inhibitors (M ± m)

Group of animals	Number of animals	NA	Dopamine
Oil	6	2,28±0,21 (5)	1,46±0,17 (5)
TP + AT[a]	3	4,50±0,25*** (3)	2,50±0,35* (3)
Oil	6	2,33±0,27 (4)	1,60±0,30 (4)
TP + AT[a]	6	4,05±0,52 (4)	2,57±0,38 (4)
Oil	8	3,42±0,43 (5)	2,98±0,48 (5)
TP + AT[b]	9	4,44±0,41 (5)	1,94±0,21 (5)
Oil	10	2,76±0,57 (5)	2,48±0,43 (5)
TP + ATD[b]	11	3,52±0,57 (5)	2,14±0,25 (5)

Legend. a) Injected on 5th day; b) injected on 5th and 7th days of life.

or on the 5th and 7th days of life.* Control animals received the solvent — peach oil. The NA and dopamine content in the pooled samples (the hypothalamus from one to four animals) was determined spectrofluorometrically [2] on the 7th, 8th, 10th, and 12th days of postnatal development.

EXPERIMENTAL RESULTS

Data on the time course of the change in catecholamine concentrations in the hypothalamus of the newborn female rats after injection of TP are given in Table 1. A significant increase was found in the concentrations of NA and dopamine in the hypothalamus of the androgenized animals on the 10th day of postnatal development. The catecholamine concentrations on the 7th, 8th, and 12th days of life did not differ from the control values.

The rise of the NA concentration in the hypothalamus induced by TP was discovered previously on the 7th [10], and in the whole brain on the 10th day of life [7]. The difference in the times of the rise of NA concentration was probably connected with differences in the doses and time of administration of TP.

In experiments with aromatase inhibitors (Table 2) a single injection of 0.5 mg of AT on the 5th day after birth was found not to prevent the TP-induced increase in catecholamine concentration in the hypothalamus of 10-day-old, neonatally androgenized rats. Just as when TP was given alone, the concentration of NA (experiments 1 and 2) and dopamine (experiment 2) was significantly higher than in the control.

According to data in the literature [6], the aromatase activity after injection of one of the aromatase inhibitors (ATD) remains low for 24 h. The critical period of SDB, during which the rat hypothalamus is sensitive to testosterone, corresponds to the first week of postnatal development [1]. Incidentally, although a single injection of AT on the 5th day of life can prevent the sterilizing action of TP [4], it does not abolish the rise of the catecholamine levels on the 10th day of life due to the prolonged supply of TP from its oily solution to the body. For this reason further injections of the aromatase inhibitors were given on the 5th and 7th days of life (Table 2). It was found that two injections of 1 mg ATD and 0.5 mg of AT completely abolished the rise of the catecholamine concentrations on the 10th day of life, induced by TP. The results suggest that prevention of the rise of the hypothalamic catecholamine levels in neonatally androgenized rats under the influence of aromatase inhibitors is directly connected with the mechanism of the protective action of AT and ATP in relation to the development of anovulatory sterility. The connection discovered between metabolic aromatization of testosterone and catecholamine accumulation in the hypothalamus is in agreement with the suggested model of the neurochemical mechanisms of androgen-dependent SDB [5], according to which the role of inducers of NA accumulation is ascribed to metabolites of exogenous hormones (catechol-estrogens).

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EFFECT OF UNITHIOL AND ACETYLCYSTEINE ON LIPID PEROXIDATION AND THE ERYTHROCYTE ANTIOXIDANT SYSTEM OF SENSITIZED GUINEA PIGS

A. G. Shleikin, Yu. N. Zubzhitskii, G. A. Baskovich, V. N. Kolmakov, L. P. Rodionova, N. N. Kiseleva, I. G. Kravtsova, and I. N. Makarova

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An important place in the response of the body to foreign proteins is occupied by changes in the redox balance and antioxidant activity of the tissues [1, 7], which lead to a disturbance of membrane structure and of cell metabolism. These disturbances are manifested clearly in erythrocytes which, in the course of immunoallergic processes, are exposed to the action of antigens, immune complexes, and free radicals [2, 6]. According to the observations of several workers, modification of erythrocyte membranes in pathological processes reflects changes taking place in the plasma membranes of other cells [3], and for that reason erythrocytes can serve as a model with which to study the cellular resistance of the body as a whole. A responsible role in the resistance of the cells to the action of harmful factors is played by low-molecular-weight thiols and, in particular, by glutathione, and also by enzymes participating in its reduction [11, 12]. The thiols can exert a direct action on the reactions of immunity [8] and they are components of immunocorrective agents [5]. There is evidence that acetylcysteine influences allergic reactions in man and animals [15].

In connection with the development of the microbiological production of forage proteins the probability of human development of hypersensitivity to yeast-like fungi is increased, and for that reason the study of the mechanism of action of thiols in experimental sensitization is an urgent problem, and the investigation described below was undertaken in order to study it.

EXPERIMENTAL METHOD

Experiments were carried out on guinea pigs of both sexes weighing 400-450 g. The animals were divided into two equal groups. Animals of group 1 were sensitized by a single subcutaneous injection of a suspension of a heat-killed and dried culture of *Candida maltosa* in physiological saline, equivalent to 30 mg/kg body weight. Animals of group 2 were given an equal volume of physiological saline. Each group was divided into three subgroups, each consisting of six animals. Guinea pigs of the first and second subgroups were given intra-

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