do not give rise to any such changes [3]. On the basis of these results NPY can be regarded as an important neuroendocrine modulator, closely linked with the catecholaminergic systems of the body. It can accordingly be postulated that the behavioral effects recorded in response to central injection of low doses of NPY may be connected with activation of the catecholamine systems of the diencephalon, which is most marked in the hypothalamic region.

LITERATURE CITED

1. J. T. Clark, A. Sahu, P. S. Kalra, et al., Regulatory Peptides, 17, 31 (1987).
2. K. Fuxe, L. F. Agnati, A. Härfstrand, et al., Acta Physiol. Scand., 118, 189 (1983).
3. A. Härfstrand, P. Eneroth, L. Agnati, and K. Fuxe, Regul. Pept., 17, 167 (1987).
4. T. Hökfelt, D. Millhorn, K. Seroogy, et al., Experientia, 43, 768 (1987).
5. G. A. Humphreys and W. L. Veale, Can. J. Physiol. Pharmacol., 65, 156 (1987).
6. R. F. Parrott, R. P. Heavens, and B. A. Baldwin, Physiol. Behav., 36, 523 (1986).
7. K. Tatemoto, Proc. Natl. Acad. Sci. USA, 79, 5485 (1982).
8. C. Wahlestedt, G. Skagerberg, R. Ekman, et al., Brain Res., 417, 33 (1987).
9. I. Zini, E. Merlopich, K. Fuxe, et al., Acta Physiol. Scand., 122, 71 (1984).

HYPOTHALAMIC SEROTONIN CONCENTRATION IN ADULT MALE AND FEMALE AND NEONATALLY CASTRATED MALE RATS

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The concentration of serotonin and the rate of its synthesis in the brain of sexually mature male rats are significantly lower than in the corresponding female brain [8, 15, 16]. The principal target region for sex hormones in the brain is the hypothalamus — the regulating center of the gonadotrophic function of the pituitary gland [11]. Sex differences in serotonin concentration in the hypothalamus have been found by some workers [3, 5] during the first few days after birth. It has been suggested that sexual dimorphism in serotonin metabolism begins to appear during the "critical period" of sexual differentiation of the brain. However, the role of sex hormones in differentiation of the serotoninergic system of the brain has not been explained.

The aim of this investigation was to study the character of changes in the serotonin level in the anterior (cyclic center) and mediobasal (tonic center regulating gonadotrophic secretion) hypothalamus of adult rats after blocking the action of testicular hormones on it from the first day of postnatal life.

EXPERIMENTAL METHOD

Experiments were carried out on Wistar rats aged 3-4 months: females in the diestrus stage (D1 and D2), intact and neonatally castrated males. The animals were killed at 3-4 p.m.

The concentration of serotonin (5-hydroxytryptamine; 5-HT) was studied separately in the anterior hypothalamus, including the preoptic region, and the mediobasal hypothalamus. 5-HT was determined by fluorometry of its condensation products with orthophthaleic aldehyde [2]. Fluorescence was measured on the MPF-4 spectrofluorometer (Hitachi, Japan) using excitation at 360 nm and emission at 457 nm.

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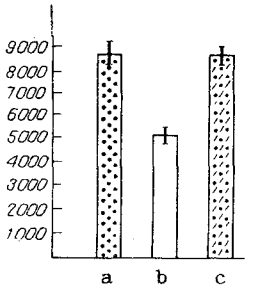

Fig. 1

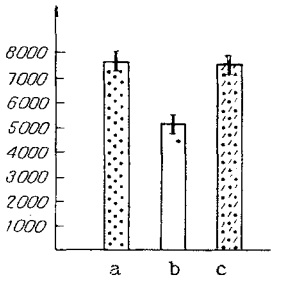

Fig. 2

Fig. 1. 5-HT concentration (in ng/g tissue) in anterior hypothalamus of female (a) and male (b) rats and neonatally castrated males (c).

Fig. 2. Serotonin concentration in mediobasal hypothalamus of female (a) and male (b) rats and neonatally castrated rats (c).

EXPERIMENTAL RESULTS

The 5-HT concentration in the anterior hypothalamus of the male rats was 5320 ± 422, and in the females 8846 ± 385 ng/g body weight, i.e., the 5-HT level in the females was 67% higher than in the males (Fig. 1). In the mediobasal hypothalamus of the males the 5-HT concentration was 5216 ± 346, and in the females 7695 ± 421 ng/g, i.e., 46% higher than in the males (Fig. 2).

It was also found that the 5-HT concentration in the anterior hypothalamus of female rats is 15% higher ($p < 0.05$) than in the mediobasal hypothalamus, whereas in males the 5-HT level in the anterior and mediobasal hypothalamus was identical (5320 ± 422 and 5216 ± 346 ng/g respectively).

Data in the literature on the 5-HT concentration in the hypothalamus are contradictory in character. The reason is evidently that 5-HT was determined in animals of different ages and at different times of the year and day. The 5-HT concentration in the hypothalamus in both males and females is known to vary not only during the period of development [4, 7], but also considerably during the 24-h period [10], and in females, additionally, it depends on the stage of the estrous cycle [1].

In adult males castrated on the first day after birth the 5-HT concentration was increased to 8813 ± 412 ng/g in the anterior hypothalamus (Fig. 1) and to 7599 ± 447 ng/g in the mediobasal hypothalamus (Fig. 2), i.e., it became the same as in females in the corresponding parts of the hypothalamus. In other words, the results are evidence that blocking the action of testicular hormones on the brain from the first day after birth leads to a significant increase ($p < 0.001$) in the 5-HT concentration in both the anterior and the mediobasal hypothalamus, to the level observed in females.

The results are in good agreement with those of the only investigation in which the 5-HT concentration was determined in the hypothalamus of adult neonatally castrated males [12]. The authors cited found by high-performance liquid chromatography that castration of newborn rats leads to a significant rise of the 5-HT level in the hypothalamus of these animals at the age of 120-180 days.

In the opinion of some authorities, sexual dimorphism in the brain 5-HT level in rats begins to appear soon after birth [3, 6, 7, 9]. For instance, it has been found [3] that the 5-HT concentration in the hypothalamus of 7-day-old females is significantly higher than in males. Furthermore, the same worker showed that the 5-HT concentration in the hypothalamus is clearly dependent on the level of androgenic saturation of the body, coinciding with the "critical period" of sexual differentiation of the brain: injection of testosterone propionate into 3-day-old females was accompanied by a significant fall of the 5-HT level in the hypothalamus of 7-day-old animals. Castration of newborn animals also led to significant rise of the 5-HT level, but only in the amygdala and corpus striatum, and was accompanied by very small changes in the 5-HT level in the hypothalamus of 12-day-old rats [12]. The question whether the sex hormones of neonates induce permanent changes in the serotoninergic system thus remains open. An important contribution to its elucidation is made by studies of the distribution of serotoninergic structures in the hypothalamus of sexually mature males and females and neonatal androgenized female rats [13, 14]. These experiments showed that the density of immunoreactive serotoninergic structures in the medial preoptic nucleus is significantly higher than in males [13]: injection of testosterone propionate into females in the perinatal period of development, however, leads to complete

reversal of the character of distribution of serotoninergic fibers in the preoptic nucleus of 3-month-old animals. Meanwhile, castration of adult males causes virtually no change in the number of serotoninergic elements in the hypothalamus [14].

It can thus be postulated on the basis of the analysis of these data that male sex hormones exert a significant influence on differentiation of the brain serotoninergic system.

LITERATURE CITED

1. V. N. Babichev and E. I. Adamskaya, Probl. Éndokrinol., 22, No. 4, 44 (1976).
2. B. H. Manukhin, E. V. Volina, L. N. Markova, et al., Zh. Évol. Biokhim. Fiziol., 16, No. 2, 105 (1980).
3. N. D. Nosenko and A. G. Reznikov, Probl. Éndokrinol., 24, No. 6, 69 (1978).
4. E. I. Plekhova, Probl. Éndokrinol., 32, No. 2, 51 (1986).
5. A. G. Reznikov, Sex Hormones and Differentiation of the Brain [in Russian], Kiev (1982), p. 147.
6. D. Giulian, L. A. Pohorecky, and B. S. McEwen, Endocrinology, 93, 1329 (1973).
7. C. M. Hardin, Brain Res., 62, 286 (1973).
8. M. Hyyppä and U. K. Rinne, Acta Endocrinol. (Copenhagen), 66, 317 (1971).
9. W. Ladosky and L. C. J. Gaziri, Neuroendocrinology, 6, 168 (1970).
10. L. Macho, R. Kvetnansky, J. Gulman, and M. Fickova, Exp. Clin. Endocrinol., 88, 142 (1986).
11. M. Sar and W. E. Stumpf, Endocrinology, 92, 251 (1973).
12. A. Siddiqui and D. P. Gilmore, Neuroscience, 22, Suppl. 154 (1987).
13. R. B. Simerly, L. W. Swanson, and R. A. Gorski, J. Comp. Neurol., 225, 151 (1984).
14. R. B. Simerly, L. W. Swanson, and R. A. Gorski, Brain Res., 340, 91 (1985).
15. A. Vaccari, S. Brotman, J. Cimino, and P. S. Timiras, Brain Res., 132, 176 (1977).
16. A. G. Watts and H. F. Stanley, Neuroendocrinology, 38, 461 (1984).