DIFFERENCES IN THE RATE OF ESTABLISHMENT OF PERMANENT ESTRUS IN RATS AFTER OVARIAN AUTOGRAFTING AND CERTAIN PROCEDURES

M. D. Smetanina and P. A. Vunder

UDC 591.147.83:599.323.4

KEY WORDS: rats; estrus; continuous illumination; cyclic center.

Age differences are found in the establishment of permanent estrus (PE) after ovarian autografting into the ears, i.e., into an environment with a lower temperature, when the level of secreted estrogen is depressed [1]. Analysis of the mechanisms responsible for these differences led to the hypothesis that age changes take place in reactivity of the cyclic center to the stimulating effect of the female sex hormone. In rats with a body weight of 200-220 g and with an estrous cycle this reactivity of the cyclic center is lower than in young (weighing 50-70 g) animals. The lower sensitivity of the cyclic center to the stimulating effect of estradiol, in our opinion, is the main cause of the rapid (after only 6-7 days) formation of PE in adult rats after transplantation of the ovaries into the ears. In young animals under the same conditions PE does not develop until several months after transplantation, when the animals' body weight is 200-220 g.

If our explanation of the mechanisms of age differences in PE formation as a result of transplantation of the ovaries into the ears is correct, the existence of similar age differences in the formation of CE of different etiology, due to round the clock illumination, for example, can be expected. The aim of the present investigation was to test this hypothesis.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino rats of two groups: on adult animals with normal estrus cycle and a body weight of 200-220 g, and on young rats weighing 90 g. Rats of the two groups were exposed to continuous illumination from luminescent lamps (250-300 lx). Some animals remained under natural conditions of light and darkness and served as the control. In a separate series of experiments continuous illumination was combined with autografting of the ovaries into the ears by the method described previously [2]. Vaginal smears were taken from all animals. The experiments were carried out in the spring and summer.

EXPERIMENTAL RESULTS

Transferring adult female rats to continuous illumination caused cessation of the sex cycle and establishment of PE after 6-7 days. A different picture was observed in the groups of younger rats. Despite transfer to continuous illumination, the sex cycle continued. After 2 months of exposure the stage of estrus was observed to be lengthened (from 1.74 ± 0.15 days in the control to 2.95 ± 0.35 days). Not until the animals' body weight had reached 200-220 g, i.e., after 3 months, was PE established. These data agree with the results of experiments [9] which showed that PE developed more rapidly in rats exposed to continuous illumination after the age of 30 days than in animals exposed to this factor at the age of 16 days. The authors cited consider that differences in the times of establishment of PE which they observed were due to the fact that with earlier exposure to continuous illumination the animal became adapted to light and formed new synapses [7]. The animal is thus able, as it were, to resist the action of continuous illumination on the sex cycle. Continuous illumination, which

Department of Human and Animal Physiology, N. G. Chernyshevskii Saratov Univerity. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 9, pp. 341-342, September, 1985. Original article submitted October 30, 1984.

0007-4888/85/0009-1253$09.50

TABLE 1. Effect of Ovarian Transplantation into the Ears, Continuous Illumination, and a Combination of Both Factors on the Rate of Formation of PE in Rats

Factors to which exposed	Number of animals	Time of formation of PE, days
Continuous illumination	10	55,30±1,30
Ovarian autografting into ears	10	62,80±1,52 $P<0,005$
Ovarian autografting into ears + continuous illumination	10	30,30±1,73 $P<0,001$

acts primarily on the hypothalamus, reduces the sensitivity of the cyclic center to the estrogen [5]. Preovulatory release of luteinizing hormone (LH) is weakened or absent altogether. Ovulation does not arise. PE is established. This is what happens in adult females. In younger rats the decrease in sensitivity of the cyclic center to the stimulating effects of the estrogen under the influence of continuous illumination is manifested less strongly because of the higher initial reactivity of the cyclic center. As a result, PE is not formed. It is established later, as the animals reach maturity, and the sensitivity of their cyclic center falls with age. It was interesting to study the effect of a combination of continuous illumination and autografting of the ovaries into the ears. If our ideas on the mechanisms of PE formation are correct, during continuous illumination combined with transplantation of the ovaries into the ears summation of the two effects might be expected: reduced reactivity of the cyclic center to the estrogen, caused by continuous illumination, and a lowered level of estrogen secretion by the transplanted ovary. In this case PE may be formed earlier than after exposure to one factor alone. Our expectations were fully confirmed.

Experiments were carried out on young animals weighing 90 g with an established cycle. They showed (Table 1) that PE was established earlier in the group of rats exposed to continuous illumination than in animals with autografting of the ovaries ($P < 0.005$). The combined action of these two factors accelerated PE formation even more ($P < 0.001$) compared with animals exposed to only one factor (Table 1).

Our views on the mechanism of age differences in the formation of PE shed some light on the well known fact that after neonatal injection of small doses of testosterone into female rats PE subsequently does not appear at once. It is preceded by a period of a normal cycle in the androgenized females [3, 4, 8]. The following explanation for this phenomenon may be suggested. Neonatal androgenization with small doses of testosterone weakens the reactivity of the cyclic center to the stimulating action of estrogen. However, this effect can be manifested to the full only in the adult stage, when it is accompanied by a parallel decrease in sensitivity of the cyclic center to estradiol with age. These two factors, depressing reactivity of the cyclic center, undergoes summation, and this leads to absence of release of LH and of ovulation and to the formation of PE. It can be concluded from these results that age differences in induction of PE of varied etiology are based ultimately on the same mechanism: an age decrease in sensitivity of the cyclic center to the excitatory action of estrogen. This lowering of sensitivity arises in the reproductive period and it may be due to an age decrease in the concentration of hypothalamic estradiol receptors [10]. Age changes in the cyclic center reach their peak in old animals [6], and it is this which causes the spontaneous formation of PE that is so characteristic of old rats.

LITERATURE CITED

1. P. A. Vunder and M. D. Smetanina, Byull. Éksp. Biol. Med., No. 3, 103 (1983).
2. P. A. Vunder, M. D. Smetanina, and V. Ya. Ignatkov, Probl. Éndokrinol., No. 1, 50 (1983).

3. R. J. Ericson and V. F. Baker, Proc. Soc. Exp. Biol. (N.Y.), 122, 88 (1966).
4. R. A. Gorski, Endocrinology, 82, 1001 (1968).
5. S. Mennin and R. Gorski, Endocrinology, 96, 486 (1975).
6. J. J. Peluso, R. W. Steger, and E. S. Hafer, Biol. Reprod., 16, 212 (1977).
7. J. Ramaley, Fed. Proc., 39, 2355 (1980).
8. H. E. Swanson and J. J. van der Werfften Bosch, Acta Endocrinol. (Copenhagen), 45, 1 (1964).
9. Y. Takeo, K. Shirama, K. Shimizo, et al., Endocrinol. Jpn., 22, 453 (1975).
10. P. M. Wise and P. Camp, Endocrinology, 114, 92 (1984).

CONTROL OF THE LEVEL OF UNUSUAL ESTROGEN-BINDING PROTEIN IN RAT LIVER BY SEX STEROIDS AND THE PITUITARY

O. V. Smirnova, T. G. Vishnyakova, and V. B. Rozen

UDC 612.352.3.014.467:577.175.64]-06:[612.616.31+612.433

KEY WORDS: sex steroids; pituitary; liver; unusual estrogen-binding protein.

Unusual estroggn-binding protein (UEBP) is one component of a system of intracellular proteins of the rat liver that specifically bind sex steroids. It has been suggested that UEBP is responsible for the accumulation of biologically active sex steroids in the hepatocytes, by inhibiting their metabolism, and that it regulates the rate of their binding with the corresponding receptors [4, 8, 10, 13]. Meanwhile UEBP is a sex-dependent liver protein: it is found in large quantities (6-10 picomoles/mg cytosol protein) in the liver of male rats only, and its content in female rats is at a low (basal) level [3, 5, 6, 13]. The high UEBP concentration in the liver of sexually mature males is due to pre- or neonatal imprinting of its level by androgens (AN). Primary injection of AN into female rats in various stages of ontogeny also induces determination of a high UEBP level [6, 13].

It is not yet clear whether AN has a significant role also in the regulation of the already induced level of this protein, or what relations exist between AN and estrogens in regulation of the UEBP concentration.

A number of facts point to a role of the pituitary in the formation of sex differences in metabolic activity of many systems of the liver [1, 9, 11]. The pituitary also is essential for primary AN dependent determination of the UEBP level [6].

The aim of this investigation was to study the role of sex steroids and the pituitary in regulation of the UEBP level in the rat liver.

EXPERIMENTAL METHOD

The following groups of male rats of a mixed population were used: immature (30-40 g), prepubertal (80-90 g), mature (150-200 g), mature and castrated 15-20 days before the experiment or hypophysectomized [6] 20-25 days before the experiment, with the testes intact or removed, and also mature female rats, ovariectomized 15-20 days before the experiment. This last group was used after the following procedures: 1-3 days after induction of the UEBP level in these animals with testosterone propionate (TP), according to the scheme used previously [6], the animals were hypophysectomized, and the UEBP level was determined 20-25 days after the last operation. Nonhypophysectomized females, used at the same times after injection of TP, served as the control. Completeness of removal of the glands from rats of all groups was verified by methods described previously [6].

Hormones were injected intramuscularly in 0.4 ml of propylene-glycol per animal: TP in a dose of 3 mg daily for 3 days, estradiol (E_2) in a dose of 10 μg, once only or daily for 6

Laboratory of Endocrinology, Faculty of Biology, M. V. Lomonosov Moscow University.
(Presented by Academician of the Academy of Medical Sciences of the USSR S. E. Severin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 9, pp. 342-345, September, 1985. Original article submitted July 20, 1984.

