

EXPERIMENTAL BIOLOGY

MONOAMINE CONTENT AND ACTIVITY OF CERTAIN ENZYMES IN THE ARCUATE NUCLEUS OF THE HYPOTHALMUS IN YOUNG AND AGING RATS DURING THE ESTROUS CYCLE

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The arcuate nucleus and median eminence of the hypothalamus of young and aging female rats were investigated. In the course of the estrous cycle the monoamine (MA) content and the activity of monoamine oxidase (MAO) and NADP- and NAD-diaphorases were determined in the arcuate nucleus and the MA content and alkaline phosphatase activity in the median eminence. In young rats activity of NADP- and NAD-diaphorases and the MA content were increased and MAO activity reduced in proestrus-estrus, pointing to increased function of the nucleus in these phases of the estrous cycle. The accumulation of MA in the median eminence was observed in diestrus, but their content fell sharply in proestrus; alkaline phosphatase activity, on the other hand, rose considerably. In aging rats the dynamics of these indices was the same during the course of the estrous cycle. However, the level of functional activity of the arcuate nucleus was increased, and in the median eminence an increase in the concentration and disturbance of the liberation of MA from nerve endings were found.

KEY WORDS: estrous cycle; arcuate nucleus; median eminence; age changes.

There is no longer any dispute that primary disturbances of function of certain hypothalamic nuclei play the leading role in the genesis of age changes in the endocrine system frequently leading to specific pathological disturbances [2, 6, 12]. However, the nature of these disturbances and their morphological characteristics have been inadequately studied.

The object of this investigation was to study the functional morphology of the arcuate nucleus of the hypothalamus in the early stages of aging.

The arcuate nucleus of the hypothalamus is characterized by reception of peripheral steroid hormones [14, 15] and it is an important integrative and regulatory center of the hypothalamus [1,9, 11]. The study of the morphological and functional state of the arcuate nucleus, both during physiological fluctuations in the blood hormone level (the sex cycle in young animals) and during changes in hormonal homeostasis during age changes in the endocrine system, is thus of special interest.

EXPERIMENTAL METHOD

Experiments were carried out on young (age 4-5 months, weight 130-150 g) and aging (age 12-14 months, weight 200-220 g) female albino rats. Changes in the generative function (reduction of the litter) began in rats aged 12-14 months and the duration of their estrous cycle was increased to 7-8 days on account of lengthening of diestrus. Regular 5-day cycles were observed in the young rats. The experimental animals were kept under the same conditions with strict alternation of light (12 h) and darkness (12 h). The phases of the estrous cycle were determined from the cytological picture of vaginal smears and the histological structure of the vaginal epithelium. Additional criteria were the glucocorticoid and protein-bound iodine levels in the blood plasma [7]. At each phase of the cycle (estrus, metestrus, the first day of diestrus, and proestrus) 5 to 7 animals were chosen. The method of obtaining the material was described previously [4, 5].

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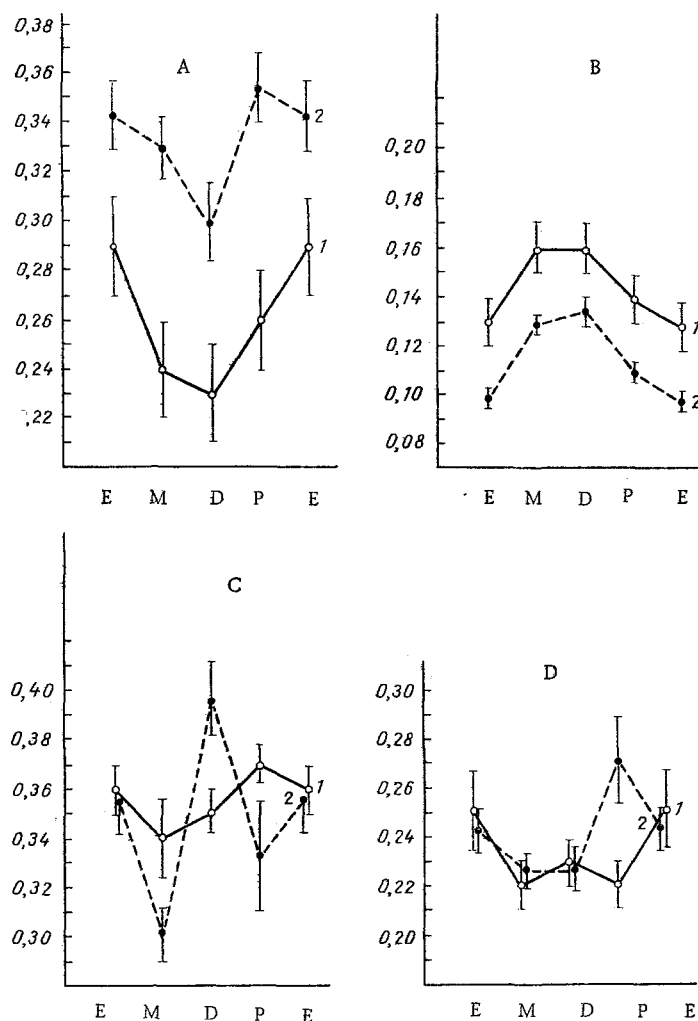


Fig. 1. Changes in MA content (A) and activity of MAO (B), NADP-diaphorase (C), and NAD-diaphorase (D) in neurons of arcuate nucleus of hypothalamus during estrous cycle: 1) young animals; 2) ageing animals. Ordinate, optical density; abscissa: E) estrus, M) metestrus, D) diestrus, P) proestrus.

The morphological and functional state of the arcuate nucleus was determined from the monoamine (MA) content in its neurons and the activity of monoamine oxidase (MAO), the enzyme of their catabolism, and of the principal energy enzymes: NAD- and NADP-diaphorases. The outer zone of the median eminence also was investigated; The MA content in the nerve terminals and alkaline phosphatase (AP) activity in the vessels of the primary plexus of the pituitary portal system were determined.

MA was detected by a modified "water" method [4] and the activity of MAO and NAD- and NADP-diaphorases with the aid of tetrazolium salt; AP was determined by the azo-coupling method [3, 8]. The activity of these enzymes was determined quantitatively by scanning a standard area of the sections with the MUF-5 dual-beam microphotometer and the MA content was determined by a "photographic" method [4]. In all sections from 30 to 50 cells (vessels) were investigated, choosing one or more values of optical density in each case. The numerical results were subjected to statistical analysis by a special [10] computer program. Values of mathematical expectancy, dispersion, and standard deviations of these values were calculated. The significance of differences between mean values were assessed with 95% confidence limits. Histograms of distribution of probabilities were analyzed and the degree of their difference determined with respect to a conventional index reflecting the minimal percentage of cells whose activity changed during the transition from one consecutive phase of the cycle to the next.

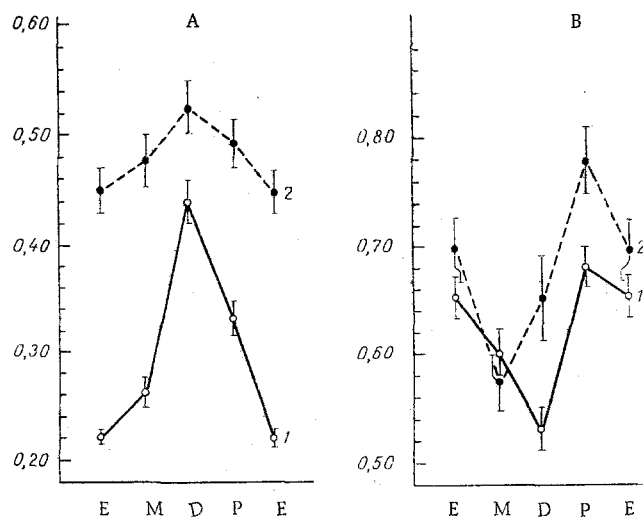


Fig. 2. Changes in MA content (A) and AP activity (B) in outer zone of median eminence during estrous cycle. Legend as in Fig. 1.

EXPERIMENTAL RESULTS

During the course of the estrous cycle considerable changes both in MA content and in the activity of the enzymes studied were discovered in the neurons of the arcuate nucleus of the hypothalamus in young rats.

The MA level was lowest in metestrus—diestrus, rose in proestrus, and reached a maximum in estrus. The dynamics of MAO activity was the opposite (Fig. 1A, B) [5]. NADP-diaphorase activity was low in metestrus, it rose a little in diestrus (not significantly), and increased considerably in proestrus—estrus (Fig. 1C). An increase in NAD-diaphorase activity was discovered in estrus and it fell in the subsequent phases (the differences between the mean values for estrus and diestrus were not significant) (Fig. 1D).

Synchronized changes were thus observed in the MA content and activity of NADP- and NAD-diaphorases in the arcuate nucleus and activation of NADP-diaphorase preceded the increase in the MA level a little. In proestrus and estrus, the synthesis and concentration of MA evidently increase consecutively, evidence of increased functional activity of the nucleus; in metestrus—diestrus, on the other hand, processes of transport and catabolism of MA predominate.

In the outer zone of the median eminence accumulation of MA was observed in diestrus, whereas in proestrus their content fell, to reach a minimum in estrus (Fig. 2A). Consequently, reciprocal relationships apply between the MA content in the neurons of the arcuate nucleus and in their terminals in the region of the median eminence. The fall in the MA level in proestrus—estrus indicates their elimination in these phases and it is accompanied by marked activation of AP (Fig. 2B), which in turn is evidence of intensified transport process in the vessels of the pituitary portal system [13].

The character of the dynamics of all functional indices studied during the course of the estrous cycle in the arcuate nucleus and median eminence of the hypothalamus was basically the same in the aging rats as in the young animals. However, in the neurons of the arcuate nucleus an increase in the total MA content was observed, and in some phases of the cycle the activity of the tissue respiration enzymes also was increased (Fig. 1A, C, D). On the other hand, MAO activity was reduced (Fig. 1B). The range of the cyclic variations in the mean values of these indices did not change significantly, but the percentage of cells whose activity changed in the course of the cycle rose sharply. The MA concentration in the median eminence also rose, but the degree of its changes in the course of the cycle was smaller (Fig. 2A). During the investigation of AP more marked activation of this enzyme was found in proestrus than in the young animals, whereas the level of its activity in the remaining phases of the cycle remained about the same (Fig. 2B).

An increase in the MA content, activation of the main energy enzymes, and a decrease in MAO activity were thus found in the arcuate nucleus of the hypothalamus of aging rats. The range of cyclic variations in the mean values of these indices was retained but these variations actually took place through a change in the functional state of a majority of the cells. These facts point to an increase in the level of functional activity and also to definite morphofunctional reorganization of the arcuate nucleus in the early stages of aging. The in-

crease in the MA content in the median eminence found in the aging rats, coupled with persistence of a relatively high MA level in proestrus-estrus, is evidence of a disturbance of the liberation of MA from the nerve endings located in this region. On the other hand, comparison of the dynamics of the MA content and AP activity in the median eminence leads to the conclusion that the change in concentration and in the range of cyclic fluctuations in MA is not reflected in the transport processes in the blood vessels of the pituitary portal system.

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EFFECT OF ANTIBIOTICS OF THE PENICILLIN SERIES ON FETAL AND NEONATAL DEVELOPMENT IN RATS

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Penicillin, if injected into rats in large doses at different stages of pregnancy, had no adverse effect on the developing fetus or the newborn rat. Meanwhile benzathine penicillin (bicillin-3) caused resorption of the embryonic cells and acted adversely on development of the heart. Consequently, benzathine penicillin must not be used for the prevention of relapses of rheumatic fever on patients earlier than in the third trimester of pregnancy.

KEY WORDS: pregnancy; benzathine penicillin; penicillin; embryonic development.

Antibiotics are widely used for the treatment and prophylaxis of rheumatic fever in pregnancy.

Meanwhile the effect of various antibiotics on the intrauterine development of the fetus is not yet completely solved.

Evidence has been obtained that certain antibiotics, which pass easily through the placenta and also through the mother's milk, adversely affect the fetus and newborn infant [1-5].

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