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BRAIN NORADRENALIN LEVELS IN RATS OF DIFFERENT AGES AFTER ADAPTATION TO A NEW ENVIRONMENT AND PASSIVE AVOIDANCE LEARNING

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KEY WORDS: noradrenalin; brain; stress; passive avoidance learning; ontogeny.

Significant changes in plasma 11-hydroxycorticosteroid (11-HCS) levels were found previously [2, 3] in rats of different ages after adaptation to a new environment and after passive avoidance learning (PAL).

Considering the close interaction between the pituitary-adrenal system and central adrenergic structures [4, 6], it was decided to study the effect of the above procedures on brain noradrenalin (NA) levels in rats of the same age groups.

EXPERIMENTAL METHOD

Male Wistar rats (90 aged 1 month, 88 aged 2 months) were used. Daily for 7 days the animals were placed for 3 min in a large illuminated compartment of a PAL apparatus, from which they spontaneously emerged through a round hole into a small, dark compartment (inborn preference for dark, small places). On the 8th day after the rats had remained for 3 min in the small compartment the hole was closed, and in the course of 1 min 20 bursts of ac pulses (50 Hz, 1 mA, duration of burst 0.5 sec) were applied to the grid floor. The presence of PAL (the animal did not move from the large into the small compartment during 3 min) was tested 24 h after electric foot shock (EFS). NA concentrations were determined fluorometrically by the trihydroxyindole method [5] in two parts of the brain: cortico-striatal (cerebral cortex, hippocampus, corpus striatum) and hypothalamus–brain stem (hypothalamus, thalamus, preoptic region, corpora quadrigemina). The brain was removed after decapitation of the animals in the animal house (basal NA level) or in the experimental room. The experimental results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

Comparison of the weight of the two brain regions studied in animals of both age groups showed that the hypothalamus–brain stem division of the brain develops much more rapidly than the cortico-striatal. The weight of the first brain division was 22.3% greater in rats aged 2 months than in those aged 1 month, whereas the weight of the second brain division was only 9.4% greater (285.0 ± 3.4 and 233.0 ± 2.1 mg, $P < 0.001$; 965.0 ± 8.5 and 882.0 ± 5.4 mg, $P < 0.001$, respectively). The rise in the basal NA level with age, on the other hand, was greatest in the unadapted animals in the cortico-striatal division (Fig. 1), in which it amounted to 65% ($P < 0.001$) compared with 34% ($P < 0.05$) in the hypothalamus–brain stem. Whereas in unadapted rats aged 1 month the NA concentration in the hypothalamus–brain stem division was almost 3 times higher than that in the cortico-striatal division, in animals aged 2 months it was only twice as high. Age changes in NA levels discovered in the different parts of the brain agreed with data in the literature [9, 12], according to which ontogenetic maturation of central noradrenergic pathways takes place in a strictly caudal-rostral direction, reflecting growth of axons and terminals from noradrenergic neurons from the brain stem.

Neither a new situation nor adaptation to it for 1 week (Fig. 1) led to any significant change in the NA level in the two brain divisions in rats aged either 1 month or 2 months. No changes likewise were found in the NA levels in animals of the two groups 15 min after EFS.

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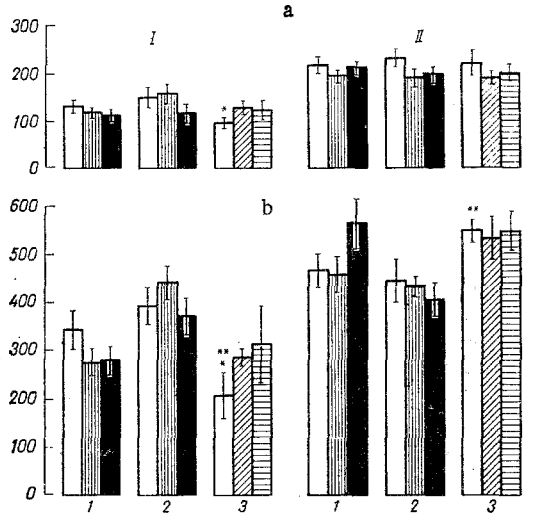

Fig. 1. NA concentration (in ng/g wet weight of tissue) in cortico-striatal (a) and hypothalamus–brain stem (b) brain divisions in rats of different ages after adaptation to a new environment and PAL. I) Rats aged 1 month; II) rats aged 2 months. 1) Unadapted rats; 2) 24 h after a 7-day period of adaptation to the small compartment; 3) adapted rats, 24 h after EFS. Unshaded columns – control (basal level); vertically shaded columns – after a stay of 3 min in the small compartment; black columns – 15 min after EFS; obliquely shaded columns – absence of PAL; horizontally shaded columns – presence of PAL. Each column represents statistical mean value for data obtained on 8-11 rats. *P 0.5 compared with basal NA level in adapted rats, **) the same, compared with NA level in adapted rats 15 min after EFS.

Meanwhile changes in the basal NA level were found in rats of both age groups 24 h after EFS. In the younger group it was significantly lower than in adapted animals in both divisions of the brain: by 38% in the cortico-striatal ($P < 0.05$) and by 46% in the hypothalamus–brain stem ($P = 0.01$) division. In the latter division the NA level fell by 42% ($P = 0.02$) relative to its concentration observed 15 min after EFS also. Conversely, in rats aged 2 months the basal NA level 24 h after EFS was raised by 35% ($P < 0.01$), but only in the hypothalamus–brain stem division and only relative to its level 15 min after application of EFS.

The fall in the brain NA level in acute stress, it has been suggested, is linked with its more intensive enzymic degradation due to increased activity of catechol-o-methyltransferase [1] or of monoamine oxidase [7]. The increase in the brain NA concentration can evidently be connected with lowering of the activity of these enzymes or with increased activity of the enzymes of NA biosynthesis.

The writers found previously [2, 3] that the plasma 11-HCS level 24 h after EFS was raised in rats aged both 1 and 2 months in the absence of PAL, but was unchanged in its presence. By contrast with this parameter, the NA level in the two brain divisions in rats of both age groups did not differ significantly in animals with and without PAL (Fig. 1). This observation is in agreement with data according to which no correlation exists between the catecholamine concentration in the whole brain and preservation of the structural trace during PAL [13].

Comparison of the results of this investigation with those of previous studies [2, 3] thus shows that the plasma 11-HCS level is a more sensitive parameter of adaptation to a new situation, and of learning and memory than the brain NA level. The adrenal cortex responds more rapidly to short-term and relatively weak stress factors. The 11-HCS level is considerably raised immediately after animals are placed in a new situation or very soon after EFS for 1 min, whereas the brain NA level remains unchanged under these conditions.

It must be emphasized that, unlike other investigators, we used weak, short-acting nociceptive stimuli. Perhaps for that reason we did not observe the rapid fall of the NA level,

found by these investigators either in the whole brain or in its two divisions, accompanying intensive and prolonged EFS [7, 8, 10, 11]. Meanwhile, 24 h after EFS, which we used to induce PAL, we found significant changes in the brain NA level, which were opposite in direction in animals of different age groups. The substantial fall in the basal NA level in both parts of the brain studied after very weak and short-acting stress in rats aged 1 month can be regarded as evidence that these animals were more sensitive to stress than rats aged 2 months, in which the NA level not only did not fall, but actually rose in the hypothalamus–brain stem division.

These results indicate differences in reactivity of the brain catecholaminergic systems to injury in rats of different ages.

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MECHANISM OF PARTICIPATION OF BONE MARROW CELLS IN COAGULATION

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KEY WORDS: bone marrow; fibronectin; culture; factor VIII antigen.

The role of the cellular factors of coagulation in the manifestation of the functional properties of the hemostasis system is regarded as exceptionally important [1, 3, 4]. Ability of the blood to coagulate is known to be determined by the functional state of the plasma membranes of the blood, blood vessel, and tissue cells. The problem of relations between the cellular component of the hemostasis system and the plasma component has been discussed in detail in the literature, but only a few publications have dealt with the participation of bone marrow cells in coagulation processes [7-9].

The aim of this investigation was to study the coagulatory and lytic properties of bone marrow in rats and changes in the concentration of fibronectin and factor VIII antigen in the culture medium of mouse bone marrow cells after 1 to 8 weeks in culture.

EXPERIMENTAL METHOD

Experiments were carried out on 30 male Wistar rats weighing 180-200 g. Under ether anesthesia the bone marrow was removed from the femur and tibia, suspended in cold buffered physiological saline, and then washed 3 times at 2000g for 10 min. Blood was taken from the animals' jugular vein and treated under similar conditions. The blood and bone marrow cells were counted, a cell suspension with a concentration of $(6\text{-}8)\cdot10^{12}$ cells/liter was prepared, and this was used in the experiments in a dilution of 1:10. Some blood and bone marrow cells were destroyed to determine fibrinolytic activity. The cells were destroyed by means of ultrasound in an MSE disintegrator (England) for 12 sec, followed by centrifugation at 8000g for 10 min. Protein was determined in the supernatant. The coagulation properties of the

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