EFFECT OF PRELIMINARY NEUROSENSITIZATION OF RATS ON POSTNATAL DEVELOPMENT OF THE CEREBRAL CORTEX IN THE PROGENY

G. F. Konokotina

UDC 612.65'825.017.3

The cerebral cortex of young rats aged 30 days born of animals previously neurosensitized with homologous cerebral cortical antigens and of intact animals was investigated. A decrease in the width of the sensomotor area was found compared with the control, mainly on account of the lower layers; the cell bodies of the large neurons were reduced in size in layer V, their cytoplasm was incompletely developed, and the accumulation of basophilic material in the cytoplasm was retarded.

KEY WORDS: preliminary neurosensitization; progeny; cerebral cortex; postnatal development.

An important problem in the pathogenesis of mental diseases is the effect of neuroautoimmune processes in the mother on the neuro-ontogeny of the progeny [8]. In particular, the presence of antibrain antibodies in the maternal blood during pregnancy is known to be connected with retardation of the child's mental development [4, 9]. Experimental studies have shown that maternal neuroimmunization leads to the inhibition of differentiation of individual nerve tissue structures in the fetus [12, 14]. However, the morphological features of postnatal development of the nervous system whose neuroembryogenesis took place against the background of neuroautoimmune conflict has hardly been studied.

This paper presents some morphological data on the effect of preliminary neurosensitization of rats on the postnatal development of the cerebral cortex of the progeny.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino rats. A 20% physiological solution of cerebral cortical isoantigen in a dose of 0.3 mg/200 g body weight was injected intraperitoneally 3 times at intervals of 24 h. On the 21st day after the 1st injection of antigen the rats were mated with healthy males. The presence of antibrain antibodies in the blood of the neurosensitized female rats was determined by the complement fixation test in the cold. The young rats were born on the 21st-22nd day of pregnancy. Rats of the same age born of intact animals served as the control. The number of rats in the litter of the control and experimental rats was identical. On the 30th day after birth the young rats were decapitated. The brains of 14 experimental and 14 control young rats were fixed in Carnoy's fluid and then embedded in paraffin wax. The width of the sensomotor area of the cortex and the separate width of the upper (I-IV) and lower (V-VII) layers were measured in serial sections 10 μ thick, stained with thionine by Nissl's method, by means of a linear ocular-micrometer. The areas of cross-section of the body, nucleus, and cytoplasm of the large neurons in layer V in this area of the cortex were calculated in 5 control and 5 experimental rats (for 50 neurons in each animal). The results were subjected to statistical analysis (they are shown in Tables 1 and 2 without a correction factor for shrinking). The brains of 9 control and 9 experimental young rats were fixed in formalin and embedded in celloidin for histological examination.

EXPERIMENTAL RESULTS

No gross disturbances of the cytoarchitectonics were found in the cerebral cortex of the 30-day-old rats obtained from preliminarily neurosensitized females, and the structure of the layers was distinct. However, neurons of all layers of the cortex were paler than in the control material. Their cytoplasm was deficient in

Laboratory of Pathological Anatomy, Moscow Research Institute of Psychiatry, Ministry of Health of the RSFSR. (Presented by Academician of the Academy of Medical Sciences of the USSR, A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 7, pp. 89-91, July, 1978. Original article submitted January 5, 1978.

TABLE 1. Width of Sensomotor Cortex of 30-Day-Old Control and Experimental Rats

Parameter	Control (M ± m)	Experiment (M ± m)	Percent of control, taken as 100	P
Mean width of cortex, mm	1,360±0,047	1,240±0,096	91,3	<0,001
Mean width of layers I, II, and III, mm	0,580±0,033	0,550±0,048	98,3	>0,4
Mean width of layers V, VI, and VII, mm	0,780±0,043	0,690±0,053	92,8	<0,001

Legend. Fourteen animals each in experimental and control groups; number of measurements 84.

TABLE 2. Changes in Area of Cross Section of Body, Cytoplasm, and Nucleus of Large Cells in Layer V of Sensomotor Cortex of 30-Day-Old Experimental and Control Rats

Parameter	Control (M ± m)	Experiment (M ± m)	Percent of control taken as 100	P
Area of cross section of cell	253,4±5,7	211,4±5,5	83,1	<0,001
Area of cross section of cytoplasm	143,8±2,7	115,1±2,8	80,0	<0,001
Area of cross section of nucleus	109,7±2,8	102,4±2,2	93,3	>0.05

tigroid, which was mainly located near the nucleus, or sometimes above the nucleus in the form of a "cap." Most cortical neurons of the experimental animals, unlike the control, were pear-shaped and the basal dendrites of the majority of cells could not be examined. Single nerve cells with pathological changes also were found: indistinctness of the cell outlines, hyperchromatosis, shrinking of the nuclei, and sometimes the cytoplasm at the periphery had a worn-out appearance.

The total width of the sensomotor cortex was 8.7% less than in the control ($P < 0.001$), mainly on account of a decrease in the width of the lower layers of the cortex (Table 1).

Measurement of the area of cross section of the large cells in layer V showed a decrease in size of the cell bodies by 16.9% ($P < 0.001$) compared with the control, mainly on account of a decrease in area of the cytoplasm (Table 2).

It can thus be concluded from the results of this investigation that preliminary neurosensitization of rats with cerebral cortical isoantigen before pregnancy causes delayed development of the cerebral cortex in the progeny. This is reflected in the fact that 30 days after birth the width of the cortex and the size of the cell bodies of the cortical neurons are reduced, the cytoplasm is inadequately developed, and the accumulation of basophilic material in it is retarded. The character of distribution of the basophilic material in the experimental animals reflects an earlier stage of tigroid formation in the cytoplasm of the neurons in the course of neuro-ontogeny [7]. The degree of underdevelopment was well-marked in the deep layers of the cortex (V-VII), suggesting that the noxious agent has an intrauterine influence on neuroembryogenesis of the cortex, for the formation of the large long-axonal cells is known to be completed in the prenatal period.

The mechanism of the effect of neuroautoimmune reactions during pregnancy on the fetus has not yet been fully explained. According to recently published data, immunologic reactions are ascribed a role in the mechanisms connecting the homonymous organs and systems of mother and fetus [1, 3]. Considering the increased natural physiological sensitization of the mother during the period of fetal morphogenesis [2], it can be postulated that neurosensitization of the mother in the present experiments before pregnancy may act as a stimulator of the additional production of autoantibodies against developing brain tissue in the period of neuroembryogenesis. Autoantibodies passing through the placenta from the mother into the fetal blood [6] may have a direct inhibitory action on development of the cells of the nervous system, and has been shown in nerve tissue culture experiments [13].

LITERATURE CITED

1. M. Sh. Verbitskii, O. K. Vyazov, A. G. Bashlai, et al., Vopr. Okhr. Mat., No. 11, 46 (1971).
2. L. S. Volkova, Immunobiological Relations between Mother and Fetus [in Russian], Moscow (1970).
3. O. E. Vyazov, Vest. Akad. Med. Nauk SSSR, No. 6, 32 (1973).
4. N. T. Zubtsova, in: Fetal and Neonatal Cerebral Pathology [in Russian], Moscow (1972), pp. 13-23.
5. B. N. Klosovskii et al., in: Antinatal Care of the Fetus [in Russian], Moscow (1968), pp. 208-219.
6. M. Ya. Maizelis, S. F. Semenov, and R. D. Kogan, in: Immunology of Nervous and Mental Diseases [in Russian], Moscow (1974), pp. 311-313.

7. Z. D. Pigareva, Biochemistry of the Developing Brain [in Russian], Moscow (1972).
8. K. A. Semenova, N. T. Zubtsova, V. V. Batmanova, et al., in: Immunology of Nervous and Mental Diseases [in Russian], Moscow (1974), pp. 42-47.
9. K. A. Semenova and Z. I. Golubovskaya, Trudy Moskovsk. Nauch.-Issled. Inst. Psikhiat. Min. Zdrav. RSFSR, 54, 22 (1968).
10. J. Altman et al., J. Comp. Neurol., 126, 357 (1966).
11. P. Darer, J. Hirnforsch., 15, 49 (1974).
12. S. Gluecksohn-Waelsch, J. Embryol. Exp. Morph., 5, 83 (1957).
13. A. C. Sharma et al., Ind. J. Med. Sci., 26, 45 (1972).

CYCLIC AMP METABOLISM IN THE LIVER OF NEWBORN RATS AFTER IRRADIATION DURING ORGANOGENESIS

L. V. Slozhenikina, L. P. Mikhailets, L. A. Fialkovskaya, and A. M. Kuzin*

UDC 612.65:577.491:577.1

The level of adenylate cyclase (AC) and phosphodiesterase (PDE) activity and the reserves of cyclic AMP in the liver of newborn rats were investigated in normal animals and after irradiation on the 9th day of embryonic development. After irradiation in a dose of 50 R the basal AC and PDE activity was reduced, but there was no change in the steady-state cyclic AMP content in the tissues. The adrenalin-stimulated AC activity showed only a tendency to fall after irradiation. It is suggested that at critical moments of development, when the hormonal inducer is present in the liver of irradiated animals the conditions may be created for an increase in the cyclic AMP reserves.

KEY WORDS: adenylate cyclase; phosphodiesterase; cyclic AMP; rat liver; ontogeny.

The role of cyclic AMP in the regulation of growth, proliferation, and morphological and enzymic differentiation has now been established [4-6, 8, 11]. Since these processes are disturbed by the action of ionizing radiation of the body, it is interesting to study the state of the cyclic AMP system in order to explain certain radiobiological effects.

There is evidence of the high radiosensitivity of the period of major organogenesis in the embryonic development of animals. Irradiation during this period, depending on dose, leads to a lower prenatal mortality than in the preimplantation period, so that it is possible to obtain progeny for investigation, although substantial disturbances of future development take place [9]. There is no information in the literature on cyclic AMP metabolism in newborn animals following irradiation of embryos in the period of organogenesis.

The basal cyclic AMP level and activity of enzymes of its metabolism, namely adenylate cyclase (AC) and phosphodiesterase (PDE), in the liver of newborn rats were investigated after irradiation on the 9th day of embryonic development.

EXPERIMENTAL METHOD

Wistar rats in heat were detected by vaginal smears and mated with males in the ratio of 2:1. The following morning was taken as the beginning of pregnancy for females found to have spermatozoa. The animals were irradiated on the 9th day of pregnancy in a dose of 50 R on the GUBÉ (cobalt-60) apparatus, with a dose rate of 23 R/min. The liver of newborn rats was used for the experiments.

*Corresponding Member of the Academy of Sciences of the USSR.

Laboratory of Molecular Radiobiology, Institute of Biological Physics, Academy of Sciences of the USSR, Pushchino. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 7, pp. 91-93, July, 1978. Original article submitted November 23, 1977.

0007-4888/78/8607-0939$07.50