nents (capillary endothelium, basal membrane, astrocyte vascular peduncles) which reduced its protective function. Blood-brain barrier destabilization developing during chronic liver disease may affect the penetration of cerebrotoxins and other metabolic toxins that are produced in the course of digestion and are incompletely utilized by the liver, which fact may explain the development of a hepatic encephalopathy. These data necessitate a differentiated approach to therapy with due consideration of certain factors capable of potentiating the hepatic encephalopathy, particularly hepatotoxic drugs.

REFERENCES

1. M. Bradbury, *The concept of a9 Blood-Brain Barrier.* Wiley-Interscience (1979).
2. G. Velev and G. Shumkov, *Exp. Med. Morphol.*, (Sofia), 4, № 3, 135-139 (1975).
3. D. N. Mayanskii, *The Kupffer Cell and Mononuclear Phagocyte System* [in Russian], Novosibirsk (1981).
4. A. A. Pal'tsyn and B. V. Vtyurin, *Trudy Nauchn.-Issled. Inst. im. Sklifosovskogo*, **18**, 71-73 (1978).
5. V. P. Fedorov, I. B. Ushakov, A. N. Kordenko, *et al.*, *Izv. Akad. Nauk SSSR, Ser. Biol.*, № 1, 24-34 (1989).
6. A. Fischer, *Liver Physiology and Experimental Pathology*, Budapest (1961).
7. A. W. Ham and D. H. Cormak, *Histology* , 8th ed., Vol. 3, Lippincott (1979).
8. A. M. Chernukh, I. N. Aleksandrov, and O. V. Alekseev, *Microcirculation* [in Russian], Moscow (1975).
9. V. A. Shakhlamov, *Capillaries* [in Russian], Moscow (1971).
10. K. Atermann, *Arch. Path.*, **57**, № 1, 1-11 (1954).
11. H. Moon, *Amer. J. Pathol.*, **26**, 1041-1052 (1950).
12. J. Muller, *Arch. Exp. Path. Pharm.*, **109**, 276-294 (1925).
13. I. Rhodin, *Ultrastruct. Res.*, **25**, 450-455 (1968).
14. V. Schwarzmann, *Rev. Int. Hepatol.*, 7, № 5, 387-429 (1957).
15. H. Zimmerman, *Hepatotoxicity: The Adverse Effects of Drugs and Other Chemicals on the Liver*, New York (1978).

Morphological Characteristics of the Brain in 20-21-Day-Old Rat Embryos and in 1-5-Day-Old Rats

B. Ya. Ryzhavskii and S. I. Biryukova

UDC 611.81-013.9-053.31-092.4

Translated from *Byulleten' Experimental'noi Biologii i Meditsiny*, Vol. 116, № 12, pp. 641-642, December, 1993
Original article submitted July 14, 1993

Key Words: *brain; cortex; embryos; newborns*

The character of embryogeny in the brain and its state during the neonatal period have a marked effect on the further development of this organ [8,9,13]. This, as well as the high incidence of brain pathology in newborn infants and the difficulties of its correction [4,7], explain the high level of interest in such studies. The factors which determine the degree of development of the brain, such as its weight, the thickness of the cortex, the degree of neuronal differentiation, and so on have been analyzed [1,2,5,10,11]. It has been established that these parameters are affected by genetic and environmental factors, the level of different hormones in the blood, and the supply of oxygen and nutrients to the fetus [2,5,8]. At the same time, there is scant information on the role of different factors in the regulation of brain development, and so further study of the organ in embryos and in animals at the early stages of postnatal ontogenesis is called for.

Department of Histology, Khabarovsk Medical Institute. (Presented by V. A. Trufakin, Member of the Russian Academy of Medical Sciences)

MATERIALS AND METHODS

The brains of 49 20-day-old (5 litters) and 53 21-day-old (4 litters) embryos, and of 34 1-day-old

0007-4888/93/0012-1550$12.50

(4 litters) and 40 5-day-old (7 litters) rats were studied. All animals were obtained from 3.5-5 month-old male and female albino rats kept before mating, during pregnancy, and after birth of the offspring under standard conditions in the same vivarium. Food and water were given ad libitum. Pregnant rats, their embryos, and newborns were decapitated. The term of pregnancy was determined by the day of sperm detection in the vagina, and the age of newborns by the time of birth. The animals were weighed; the brain was fixed in Carnoy's fluid and weighed on a torsion balance, and then dissected in the anterior parietal region perpendicular to the length and to surface of the left hemisphere using Svetukhina's schemes [6]. This region was embedded in paraffin and 7-μ slides were prepared. Using random sampling 1-3 hemispheres from males and from females were chosen out of 4-7 litters of each group. The slides were stained with a 1% solution of methylene blue. The width of the molecular layer of the cerebral cortex was measured using an MOV-15 ocular micrometer. In addition, the mean number of neurons in layers II and V of the cortex was determined [5]. The results were processed statistically. The specific rate of increase of the brain weight was calculating using the formula:

$$V=(M_2- M_1)/(M_1\times t),$$

where M_1 and M_2 denote the weight of the brain at adjacent time points, and t is the difference in age, expressed in days.

RESULTS

The parameters of absolute brain weight testify that this has the closest correlation with the age of the animals. The minimal weight of the organ in the older group was greater than or equal to (in 21-day-old female embryos) the maximal weight in the younger group, althought the body weight of the largest animals in the "junior" group often exceeded that of the smallest in the "senior" animals. Thus, the growth of the brain in this period of ontogenesis more strongly correlates with the calendar age than with the body weight. The correlation between the absolute brain weight and body weight is insignificant ($r=0.2$, $p>0.05$) in 20-day-old embryos; the coefficient of correlation between these parameters was $r=0.54$, $p<0.05$ in 21-day-old male embryos and $r=0.86$, $p<0.05$ in females. A positive correlation is also found in 1-day-old rats ($r=0.7$ in males and $r=0.82$ in females, $p<0.05$). In 5-day-old animals the dependence of body weight decreases and the correlation coefficient becomes 0.3 in males and 0.2 in females ($p>0.05$). It is necessary to note that all given parameters of the brain weight are obtained after its fixation in Carnoy's fluid, when it comprises 90.3% of the actual weight [12].

The relative brain weight in the groups of animals under study differed in different age groups, testifying to the absence of proportionality between the growth of the body and of the brain. Inside the groups a negative correlation (correlation coefficient from -0.68 to -0.91, $p<0.05$) was noted between the relative brain weight and the body weight. The specific rate of growth of the brain was 0.219 between the 20th and 21st day of embryogeny, 0.161 in males and 0.155 in females between the 21st day of embryogeny and the first day of life, and 0.272 and 0.289, respectively, in the interval from the 1st to the 5th day.

The data obtained attest to the existence of individual variations of brain weight inside every group studied. Moreover, it differs markedly within one litter of animals. For example, this difference reached 30 mg in 20-day-old embryos, 20 mg in 1-day-old males, 30 mg in 1-day-old females, and 127 mg and 78 mg in 5-day-old animals, respectively. A pronounced intragroup variability was found in such a parameter as the relative brain weight, the difference between the maximal and minimal levels in the majority of groups being more than 50% of the mean value.

The histological examination of the cerebral cortex showed that in the period of ontogenesis studied its thickness increases markedly and the molecular layer expands. We did not reveal any regular correlation between the brain weight and the indicated morphometric parameters in animals of one age group. Significant sex differences in the width of the cortex and its molecular layer are found only in 5-day-old animals ($p<0.05$). A decrease of the density of distribution of neurons as compared to that in 21-day-old embryos occurs at first in the second cortical layer (in 1-day-old rats) and then in the fifth layer. By the 5th day of life it has decreased approximately two-fold in both layers as compared to the 21st day of embryogeny, reflecting the growth of neurons and of their branches and an increase of the glial mass, i.e., processes characterizing the development of the cerebral cortex. The analysis of the morphometric results attests to a significant intergroup variability, just as in the case of the parameters of brain weight.

The findings yield quantitative characteristics of some parameters of brain development in albino rats in late embryonic and postnatal periods. They

testify that in rays of the same age kept under the same conditions the offspring differ significantly already in embryogeny in brain weight and in morphometric parameters of the state of the cortex, and that these differences are not leveled after birth. It may be assumed that the differences described relate to: 1) genetic differences of the animals studied; 2) individual differences of biochemical (including hormonal) parameters of the maternal blood; 3) local in utero differences in the conditions of development of embryos, including those from one litter.

REFERENCES

1. A. A. Volokhov, *Vestn. Akad. Med. Nauk SSSR*, №12, 49-53 (1978).
2. N. I. Dmitrieva and V. G. Kassil', *Arkh. Anat.*, **83**, № 9, 84-91 (1982).
3. N. I. Dmitrieva and Yu. S. Dmitriev, *Zh. Evol. Biokhim. Fiziol.*, **28**, № 4, 524 (1992).
4. V. N. Kornienko, V. I. Ozerova, and A. S. Petrukin, *Pediatriya*, № 3, 71-76 (1986).
5. B. Ya. Ryzhavskii and I. R. Eremenko, *Fiziol. Zh.*, **78**, № 5, 109-112 (1992).
6. V. M. Svetukhina, *Arkh. Anat.*, **42**, № 2, 524-530 (1962).
7. T. A. Tomberg, T. A. Tal'vik, and M. Kh.Yurisson, *et al.*, *Pediatriya*, № 9, 50-54 (1989).
8. M. V. Ugryumov, *Neuroendocrine Regulation in Ontogenesis* [in Russian], Moscow (1989).
9. R. V. Uchakina, O. A. Lebed'ko, and L. N. Nosova, *Current Topics in Pathology of Pregnancy and Infancy in the Far East* [in Russian], Novosibirsk (1989), pp.151-156.
10. S. Ciaroni, T. Cecchini, and P. Del. Yrando, *Acta Embryol. Morphol. Exp.*, **11**, №3, 171-180 (1990).
11. I. Danko and M. Zibrin, *Plzensky Lek. Sborn.*, Suppl. 63, 177-178 (1991).
12. J. Nagel and Schierdhorn, *J. Hirnforsch*, **16**, № 4,371-378 (1975).
13. A. J. Patel, R. Balazc, and A. L. Johnson, *J. Neurochem.*, **20**, № 4, 1151-1165 (1973).

Ultrastructural Changes in Liver Cells during Severe Iron-Deficiency Anemia

T. A. Ageeva, V. A. Shkurupii, T. I. Pospelova, and M. I. Loseva

UDC 616.36-018.1:616.155.194.8-036.17-076.4

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 116, № 12, pp. 642-645, December, 1993
Original article submitted June 22, 1993

Key Words: *iron-deficiency anemia; hepatocytes; endotheliocytes; Kupffer's cells; ultrastructure*

Iron-deficiency anemias are highly prevalent [2,4]. Progressive tissue hypoxia in this condition initiates membrane lipid peroxidation and lowers the level of antioxidant defense [1,11], leading to labilization of membranes, notably of lysosomal membranes [12]. This may be regarded as a risk factor associated with the use of membranotropic and lysosomotropic agents, including the iron-containing drugs [3] used in the treatment of iron-deficiency anemias. We thus considered it expedient to study the ultrastructural changes, particularly in lysosomes, occurring during iron deficiency in various cells of the liver, an organ which is highly sensitive to hypoxia and which participates in iron metabolism and in the clearance of administered lysosomotropic drugs.

Department of Pathoanatomy and Department of Hospital Therapy, Novosibirsk Medical Institute. (Presented by Yu. M. Borodin, Member of the Russian Academy of Medical Sciences)

MATERIALS AND METHODS

Blood was taken from the marginal vein of the ear every other day, 20 ml at a time, for 40-43 days in chinchila rabbits weighing 3.5 kg. The animals

0007-4888/93/0012-1552$12.50