# Effect of Piracetam Administration to Suckling Rats on Morphometry of Neocortex and Hippocamp

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The frontoparietal and parietal lobes of neocortex and hippocamp were studied in one-month-old rats, which were daily given piracetam 1000 mg/kg i.p., starting from the 5th day of life. In piracetam-treated animals, an increase in the thickness of cortex in frontoparietal lobe and of the size of neuronal nuclei both in layer V of parietal and frontoparietal lobes of neocortex, and in zones CA1-CA5 in hippocamp were observed. RNA concentration increased in neuronal cytoplasm in layer V of neocortex and in hippocamp. The brain mass, the density of neurons in the neocortex (layers II and V), the cortical thickness of neocortex in the parietal lobe did not differ in the control and experimental groups.

**Key Words:** *neocortex; hippocamp; suckling period; piracetam*

During suckling period, both brain mass (BM) and neocortex thickness increase considerably, this process being accompanied by changes in metabolism and morphology of neurons [1,7,8]. There is evidence that certain features formed during the early postnatal life are not entirely leveled in the following ontogenesis [3]. Therefore, it was interesting to study the effects of nootropic preparations, which are used in pediatry. Piracetam belongs to this group of preparations [10]. Its effects were studied mainly by neurophysiological, psychophysiological, and biochemical methods [2,4,6,11,14]. At the same time, the effect of piracetam on morphological parameters of the brain in the early postnatal period was not investigated. This problem is important from the viewpoint of factors and mechanisms regulating brain development, and may provide more insight into the action of nootropic preparations, specifically, their effects on the brain mass growth, cortex formation, and the status of neurons.

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## MATERIALS AND METHODS

Experiments were carried out on 37 rats kept under standard vivarium conditions. Piracetam (20%, daily dose 1000 mg/kg) was injected intraperitoneally into rats (7 males, 12 females) starting from the 5th day of life. At the one-month age the rats were decapitated on the next day after the final injection. The control group consisted of rats from the same litters. Seven rats of this group were injected intraperitoneally with physiological solution in an equivalent amount while eleven rats were left intact. Control and experimental animals were decapitated simultaneously. Their body weight and BM were measured. The frontoparietal lobe (FPL) and self-parietal lobe (SPL) of the left hemisphere were dissected according to [9]. Sections (7-μ thick) were stained with 1% methylene blue, hematoxylin, eosin, and gallocyanine (the Einarson method) for nucleic acids. They were used for the morphometrical studies [7,8]. The section areas of neuronal soma and CA1-CA5 hippocamp nuclei were also measured. In the layer V neurons of FPL and CA4 neurons in the

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hippocamp, the cytoplasmic RNA concentration was determined [8]. The data were processed by the methods of variation statistics. The morphometric and cytochemical indices of intact animals did not significantly differ from those in rats given physiological solution, therefore these rats were united into a single control group.

## RESULTS

Injection of piracetam did not change the growth rate of BM. In experimental male and female rats, BM weighed 1270±25.7 and 1210±25.9 mg, respectively. In the control group the respective indices were 1280± 28.7 and 1240±15.7 mg. The relative BM of the rats in these groups also did not differ significantly. Histological investigation revealed no destructive or dystrophic changes in the neocortex and hippocamp in the piracetam-treated rats. The morphometric and cytophotometric indices were not sex-dependent, so males and females were united in the same group. The width of the cortex in FPL of experimental animals was significantly greater than in the control, while for SPL this parameter did not significantly differ in both groups (Table 1). Thus, injection of piracetam differently affected the development of the neocortex zones that had different functional specialization [9,12]. There were no significant intergroup differences in the density of neurons in layers II and V of FPL and SPL (Table 1); piracetam did not affect the section area of neurons in the neocortex layer V and hippocamp. By contrast, the size of nuclei in these cells drastically increased (Table 1). Thus, these data indicate that piracetam has a certain karyotropic activity. The most pronounced increase in the nuclear section area was observed in hippocampal neurons (by 32-47% in different zones), while in FPL and SPL it was 28% and 25.6%, respectively (Table 1). Therefore, the maximum changes in the size of nuclei were observed in the cortical area responsible for consolidation of memory [13].

Study of brain homogenates by biochemical methods showed that piracetam increases the RNA and protein levels [4]. Cytochemical studies showed that 3 injections of piracetam given to adult rats during 18 h led to an increase in the protein concentration in neuronal cytoplasm both in the neocortex and hippocamp [5]. We have shown that chronic injection of this preparation to rats in the suckling period increases the RNA concentration and the size of neuronal nuclei, i.e., induces changes associated with the revealed variations of protein content [5].

Prolonged administration of piracetam during suckling period induces morphological changes in brain structures and in neuronal processes involved in the realization of the nootropic effects of this preparation [6,13]. At the same time, piracetam did not modify BM growth, although it was injected in the ontogenic period which is characterized by a very high rate of brain growth and is very important for the cortex development and functional state of neurons. Similar data we obtained with injection of insulin into 1-3-day-old rats [8]. Thus, the available data indicate that in the neonatal and suckling periods the brain growth and morphofunctional state of cortical

**TABLE 1.** Effects of Piracetam on the Brain Morphometric Characteristics in Rats

| Parameter | Control | Experiment |
|---|---|---|
| Width of cortex, μ | | |
| FPL | 1389±20 | 1506±35* |
| SPL | 1043±22 | 1016±22 |
| Number of neurons in the visual field of layer II | | |
| FPL | 122±4.3 | 123±6.5 |
| SPL | 110±5.1 | 119±5.6 |
| Number of neurons in the visual field of layer V | | |
| FPL | 88±4.2 | 85±4.5 |
| SPL | 58±2.8 | 56±2.4 |
| Section area of neuronal perikaryon, $\mu^2$ | | |
| FPL | 144±6.2 | 147±6.5 |
| SPL | 140±4.2 | 146±4.1 |
| Section area of neuronal nucleus, $\mu^2$ | | |
| FPL | 75±2.7 | 96±5.3* |
| SPL | 78±2.8 | 98±2.5* |
| Section area of neuron, $\mu^2$ | | |
| CA1 | 222±3.4 | 218±7.2 |
| CA2 | 222±3.5 | 218±9.8 |
| CA3 | 204±2.6 | 213±6.0 |
| CA4 | 217±6.0 | 212±7.0 |
| CA5 | 200±6.4 | 224±5.5 |
| Section area of neuron's nucleus, $\mu^2$ | | |
| CA1 | 81±2.6 | 92±5.1 |
| CA2 | 76±1.7 | 100±9.4* |
| CA3 | 68±3.8 | 100±6.0* |
| CA4 | 85±3.8 | 104±6.0* |
| CA5 | 81±5.1 | 107±6.4* |
| RNA concentration in neuron's cytoplasm, arb. units | | |
| FPL | 86±4.9 | 100±4.6* |
| CA4 | 127±13.3 | 161±9.8* |

**Note.** *$p<0.05$ in comparison with the control group.

neurons are regulated by different factors. The neuronal activity and degree of differentiation, on the one hand, and BM growth, on another, should not vary necessarily in parallel.

Further studies are necessary to examine the effects of piracetam in brain pathology and its long-term effects during the neonatal period.

## REFERENCES


1. G. G. Avtandilov, *Medical Morphometry* [in Russian], Moscow (1990).
2. T. A. Voronina, S. V. Krapivin, and N. N. Bogolepov, *Vestn. Akad. Med. Nauk SSSR*, No. 2, 17-27 (1978).
3. N. I. Dmitrieva, *Arkh. Anat.*, **83**, No. 9, 84-89 (1982).
4. T. L. Karaseva, Zh. N. Tsapenko, N. Ya. Golovenko, *et al.*, *Vopr. Med. Khimii*, No. 3, 81-84 (1988).
5. V. O. Klenikova, T. S. Glushchenko, S. Guneva, and Ts. Tencheva, *Fiziol. Zh. SSSR*, **68**, No. 1, 9-12 (1982).
6. T. V. Kovalev, *Nootropic Preparations* [in Russian], Volgograd (1991).
7. B. Ya. Ryzhavskii and S. I. Biryukova, *Byull. Eksp. Biol. Med.*, **116**, No. 12, 641-642 (1993).
8. B. Ya. Ryzhavskii and S. I. Ivashkina, *Ibid.*, **120**, No. 9, 305-307 (1995).
9. V. M. Svetukhina, *Arkh. Anat.*, **42**, No. 2, 31-46 (1962).
10. I. V. Sirotina and Z. D. Aleksandrova, *Eksp. Klin. Farmakol.*, **55**, No. 1, 53-56 (1992).
11. S. S. Trofimov and R. U. Ostrovskaya, *Byull. Eksp. Biol. Med.*, **121**, No. 4, 435-437 (1996).
12. A. A. Khachaturyan, *A Comparative Anatomy of the Cerebral Cortex in Humans and Primates* [in Russian], Moscow (1988).
13. F. Hucho, *Neurochemistry: Fundamentals and Concepts*, [Russian translation], Moscow (1990).
14. G. I. Shul'gina and N. V. Okhotnikov, *Zh. Vyssh. Nervn. Deyat.*, **40**, No. 4, 732-738 (1990).