Relationship between Litter Size and the Development of the Rat Brain During the Suckling Period

B. Ya. Ryzhavskii and S. I. Ivashkina

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The brain of 23-day-old rats raised in small, large, and control litters is studied. In large litters, body weight is significantly lower and the relative mass of the brain is higher than in controls. In small litters, body weight of males and females is considerably higher, while the relative mass of the brain is lower; in females, the absolute mass of the brain and of the left hemisphere is significantly higher. In rats of both sexes from small litters the weight of body, brain, and hemisphere is higher than in rats from large litters. In addition, in males from small litters the neurons of layer V are larger.

Key Words: *brain; litter size; brain cortex*

It has been found that in human fetuses and newborns brain mass increases with weight gain [1]. A similar relationship has been recorded in rats in the late embryonal and early postnatal periods. In addition, a negative correlation is found between the relative mass of the brain and body weight in rats [7]. There is evidence that by the age of one month in rats [8,9] and 5-7 years in humans [1] the brain mass (BM) is close to that of the adult brain. Therefore, it can be hypothesized that the mass of the adult brain is strongly influenced by various factors acting before this age.

On the other hand, the body weight of multiparous laboratory animals depends on the number of pups in a litter: in small litters it is higher than in large ones [6]. It was shown that in experimental very small (1-2 pups) or very large (15 and more pups) litters the animals differ in BM, rate of nerve fiber myelinization, and biochemical parameters of brain development [3,4]. These differences result from the different level of supply of mother's milk. However, the natural variability in the number of pups in a litter makes it difficult to assess to what extent BM is determined by differences in weight gain [5]. The relationship between BM and such indexes as the width of the cortex, density of neurons, and degree of their differentiation in animals from small and large litters is unknown. The present study was designed to clarify this issue.

MATERIALS AND METHODS

The brain was studied in 23-day-old rats (n=115) of both sexes obtained from 3.5-month-old females and 3-5-month-old males (12 litters). At the age of 1 day some pups from 4 litters were placed in 4 other litters to form three groups: control litters (10.5±1.0 pups, group 1), large litters (13.8±0.5 pups, group 2), and small litters (4.5±0.5 pups, group 3). All animals were maintained under the same vivarium conditions. Females received food and water *ad libitum*. The pups were decapitated at the age of 23 days. They were weighed, and the brain was fixed in Carnoy solution. The brain and the left hemisphere were weighed on a torsion balance. Pieces of brain tissue from the parietal lobe were embedded in paraffin, and 7-μ sections were cut. The preparations were stained with 1% Meth-

Chair of Histology, Khabarovsk Medical Institute

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ylene Blue and gallocyanin (after Einarson) for nucleic acids. The width of the cortex, neuron density [7], and the size of the neurons of layer V and their nuclei measured. The concentration of RNA in the cytoplasm of these cells was determined cytophotometrically (25 cells, 550 nm). The coefficients of correlation between absolute BM and body weight (r_1) and relative BM and body weight (r_2) were calculated. The data were processed by the methods of variational statistics.

RESULTS

In control litters, BM and body weight were significantly higher in males than in females, and the mass of the left hemisphere also tended to be higher in males (Table 1). There were no such differences in small and large litters. Thus, factors with a greater influence on gravimetric parameters than on sex-related characteristics were operating in these groups. In large litters, body weight amounted to 78% (males) and 92.5% (females) of that of the controls. In small litters, the figures were 135.5% and 154.1%, respectively. The differences in BM in both groups in comparison with the control were much smaller and significant only in females from small litters (13.8%). In addition, in this group the mass of the left hemisphere was significantly higher (Table 1).

The mass of this hemisphere and BM were significantly higher in rats from small litters than in those from large litters, indicating that these gravimetric parameters correlate positively with body weight. It should be noted that there was no proportionality between the rate of BM growth and weight gain during the observation period in rats with different feeding conditions. This fact is reflected by a strong negative correlation between the relative BM and body weight (Table 1). It can be assumed that under conditions of rapid weight gain (small litters) some factors (intra- or extracerebral) inhibit the growth of BM or that in control litters the rate of BM growth is the maximum possible or close to it. On the other hand, when weight gain was markedly slowed (males from large litters) there was only a tendency towards a small decrease in BM. These findings testify to a certain autonomy of the tempo of brain growth.

There were no significant intergroup differences in the width of the cortex, neuronal density in layers II and V, and cytoplasmic RNA concentration in layer V neurons. In males from small litters these cells were larger that in males from large litters. Such differences were not observed in females. There were no significant intergroup differences in the size of the nuclei of these cells in males and females. Thus, under our experimental conditions most of the above-mentioned parameters did not

TABLE 1. Morphometric Characteristics of the Brain of 23-Day-Old Rats from Large and Small Litters

Parameter	Control (group 1)		Large litters (group 2)		Small litters (group 3)	
	males	females	males	females	males	females
Body weight, g	31.3±1.2	26.6±1.1	24.4±0.6*	24.6±0.8	41.8±1.4*+	41±2.9*+
Brain mass:						
absolute, mg	1210±28.6	1133±18.7	1152±18.6	1134±22.5	1270±15.8+	1290±40.1*+
relative, mg/g	42.1±1.5	44±1.36	48.1±0.9	44.7±0.96	30.7±0.95	31.8±1.65
Mass of left hemisphere, mg	365±12.3	336±7.6	342±7.5	340±7.5	386±4.2+	399±22.3*+
Width of cortex, μ	1454±47.2	1415±31.5	1424±44.3	1360±40.2	1454±25	1438±28.9
Number of neurons in a visual field:						
layer II	8.7±0.4	8.4±0.4	8.35±0.2	9.3±0.4	9.0±0.4	8.5±0.3
layer V	2.6±0.4	2.0±0.3	2.25±0.2	2.5±0.2	2.3±0.2	2.2±0.1
Section area (arb. units):						
cells	153±7.1	153±9.4	140±2.6	151±4.5	155±5.7+	154.5±3.0
nuclei	97.3±3.3	97.8±10.0	86.9±4.5	92.7±3.3	90.6±2.8	93.5±3.3
RNA concentration in neuronal cytoplasm, arb. units	103.8±7	105±5	111.3±4.7	107.7±4.7	108±6.7	105±8.0
Correlation coefficient:						
r_1	0.627	0.766	0.877	0.588	0.682	0.97
r_2	-0.816	-0.75	-0.92	-0.798	-0.883	-0.98

Note. Differences significant in comparison with group 1 (*) and group 2 (+).

depend on changes in BM or the mass of the left hemispheres. However, since the mass of this hemisphere in rats from small litters was lower that in those from large litters, it can be assumed that given an equal thickness of the cortex, its absolute mass in the entire hemisphere is higher in rats from small litters than in rats from large ones.

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