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Litter Size, Maternal Parameters, and Brain and Body Parameters of Neonatal Rats

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Abstract. The present work is concerned with the effect of natural litter size in the rat on the brain and body parameters of individual newborns, with particular reference to those newborns that were 'outstanding' (i.e., had parameters higher than mean ± 2 SD). Correlations between litter size on one side, and length of gestation, number of stillborns, maternal weight at conception and maternal food consumption were also studied. To our knowledge, no previous report presented a similar integrated study on such a large number of rats (288 litters, 2,725 newborns) and wide range of litter size (2–17).

In previous work we have demonstrated that prenatal operative restriction of litter size leads to newborns with increased body weight and increased values of certain brain parameters, e.g. weight, and content of DNA and protein [2, 3]. These results were also corroborated by others [1, 4, 5].

The decrease in birth weight upon increase in litter size is well documented in the rabbit and in multiple births in humans. However, in rat such a correlation could not be demonstrated in the past, probably because of the too small number of cases and too narrow range of litter sizes [2].

In the present work, the animals and their nutrition regimens were as described previously [6–8]. The frequencies of litter sizes essentially followed a normal distribution curve, with a mean value of 9.45 newborns/litter.

It was found that in the rat, as well, smaller litters are associated with higher brain and body parameters, in a statistically significant fashion (fig. 1, 2, table I). Of particular importance may be the finding that the *highest* values of body weight and brain weight (fig. 2, table I) are also significantly negatively correlated with litter size. This also applies to brain DNA or cell number, which is an index of *final* cerebral neuron number because cerebral neurons essentially do not proliferate after birth. This negative correlation with litter size also applies to brain protein and the ratio protein/DNA (in-

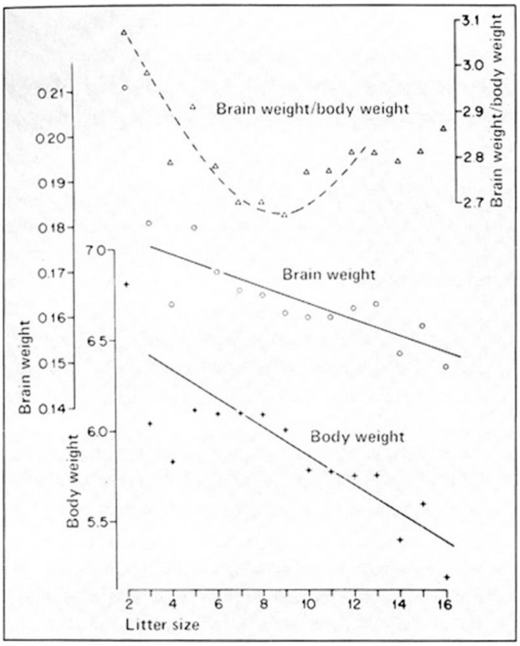

Fig. 1. *Mean* body weights, brain weights and ratios of brain weight/body weight, for all litters of the same litter size. Abscissa – litter size; ordinate – body weight, g, brain weight, g, or brain weight/body weight $\times 10^2$.

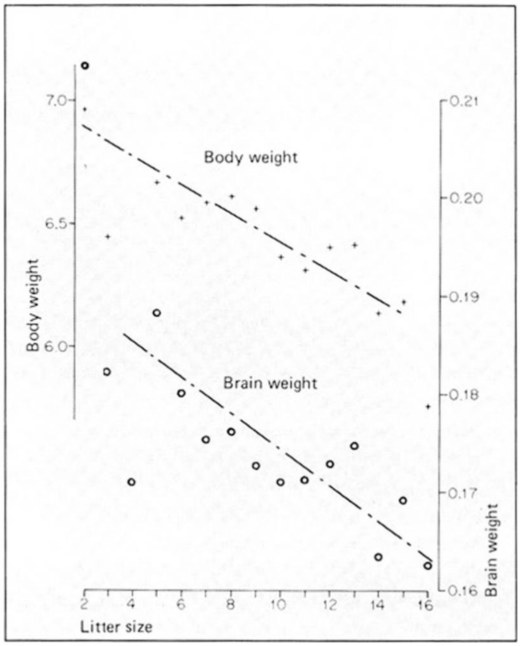

Fig. 2. *Highest* values of body weight or of brain weight in each litter: means for all litters of the same litter size. Abscissa – litter size; ordinate – means of highest body weights or of highest brain weights, g.

dex of brain cell size, table I), the two parameters that suggest the extent of postnatal brain development. We have reported previously that neonatal body weights are statistically significantly positively correlated with adolescent brain development [7]. Thus, the animals with the highest developmental potential at birth (and possibly at adolescence) are to be found in the smallest litters. These results are essentially in agreement with the results of previously mentioned prenatal operative restriction of litter size: such restriction leads to an increase in birth weight and in brain parameters of the newborns [2, 3]. Our explanation is that a smaller number of fetuses allows for more space and more nutrients for each of them. In an attempt to compensate for any space and food deficiency, maternal weight at conception and maternal food consumption increase with increasing litter size (table I). However, any such increases are very small and evidently not fully compensating for increase in litter size.

Despite the increase of both brain and body weight when litter size is decreasing, the ratio of brain weight/body weight does not remain constant but reaches a *minimum* (upper curve, fig. 1), at a litter size approximately corresponding to the mean litter size of the entire population, which is 9.45. If this litter size is most frequent because it is most advantageous for the population as a whole then, *in the rat*, the most advantageous prenatal nutrient distribution (partition) [8]

Table I. Relationships between litter size and other parameters

Parameters	r	p
Mother		
Weight at conception	+0.262	<0.0005
Average food consumption/24 h	+0.191	$0.005 < p < 0.01$
Length of gestation	−0.147	0.02
Offspring[1]		
Body weight		
Mean[1]	−0.415	<0.0005
Highest	−0.233	<0.001
Brain weight		
Mean	−0.382	<0.0005
Highest	−0.296	<0.0005
Brain		
DNA	−0.127	$0.01 < p < 0.025$
Protein	−0.311	<0.0005
Protein/DNA[2]	−0.226	<0.001

n = 288 litters; r = correlation coefficient;
p = probability value.

1 Mean (or highest) *in each litter.*

2 Protein content/DNA content is an index of cell size.

seems to favor more the body than the brain.

Although the quality of newborns (as judged by body and brain parameters) decreases with increasing litter size, the *quantity,* or body mass and brain mass (total weights per litter), linearly increases with litter size. The same is true for the ratios of body mass/maternal weight at conception, and brain mass/maternal weight. The range is very wide: the lowest body mass (litter size 2) is 5.8% of maternal body weight (possibly a pathological case), and the highest (litter size 16) is 37.6% of maternal body weight. It is likely that, at these extremes, the maternal organism will have different strategies towards destroying (resorbing) the fetuses in case of malnutrition [6], or towards building up larger fetuses (fig. 2, table I), well affordable at a low percentage of maternal body weight but not at a high percentage.

References

1 Croskerry, P.G.; Smith, G.K.; Hall, S.; Shepard, B.J.: Fetal and placental growth in the rat following differential reduction of litter size. Biol. Neonate *33:* 31–38 (1978).

2 Marthens, E. van; Zamenhof, S.: Deoxyribonucleic acid of neonatal rat cerebrum increased by operative restriction of litter size. Expl Neurol. *23:* 214–219 (1969).

3 Marthens, E. van; Grauel, L.; Zamenhof, S.: Enhancement of prenatal development by operative restriction of litter size in the rabbit. Life Sci. *11:* 1031–1035 (1972).

4 Milkovic, K.; Paunovic, J.; Joffe, J.M.: Effect of pre- and postnatal litter size reduction on development and behavior of rat offspring. Dev. Psychobiol. *9:* 365–375 (1976).

5 Wehmer, F.; Jen, K.L.C.: The effect of litter size during gestation and lactation on rat development prior to weaning. Dev. Psychobiol. *11:* 353–360 (1978).

6 Zamenhof, S.: Early prenatal malnutrition and brain development in rats; in Mittler, de Jong, Research to practice in mental retardation, vol. 3, pp. 347–354 (University Park Press, Baltimore 1977).

7 Zamenhof, S.; Ahmad, G.; Guthrie, D.: Correlation between neonatal body weight and adolescent brain development in rats. Biol. Neonate *35:* 273–278 (1979).

8 Zamenhof, S.; Marthens, E. van: Distribution of nutrients between fetal brain and body during rat development. Biol. Neonate *41:* 68–73 (1982).

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