Protein and RNA biosynthesis in various cellular fractions of the brain of undernourished rats

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Body and brain weight; DNA, RNA, and protein content; total free nucleotides; amino acids and their specific activities; as well as the in vitro incorporation of ^{14}C-phenylalanine into protein and of ^{3}H-orotate into RNA of homogenates and various cellular brain fractions were measured in well-fed (WF) and undernourished rats during gestation (EI) and during growth, gestation, and lactation (EII). Body weight was significantly decreased in both EI and EII while brain weight and DNA content per organ were lower in EII than in WF and EI rats. The brain weight:DNA ratio was increased significantly in EII animals compared with the WF group. RNA content did not show any significant alterations in homogenates, nuclear, microsomal and pH-5 enzyme fractions but was elevated in mitochondrial and soluble fractions of the brain of EI rats compared with the WF group. Brain RNA content in EII animals was decreased in homogenates and all cellular fractions with the exception of the nuclear fraction in which it did not change significantly. The RNA:DNA ratio tended to increase (non-significantly) in the EI and EII groups as compared with the WF controls. Protein content was decreased in homogenates and all cellular fractions of EII rats while it was reduced only in the mitochondrial and pH-5 enzyme fractions of the EI group. The RNA:protein ratio fell in the microsomal fraction and rose in the soluble and pH-5 enzyme fractions of EI and EII animals. The protein:DNA ratio increased significantly in homogenates and the nuclear fraction of the EII Group: ^{14}C-phenylalanine/mg protein incorporation was augmented in homogenates, mitochondrial, and soluble fractions, was diminished in the microsomal fraction, and did not change in the nuclear fraction of the brain of EI and EII rats. ^{3}H-Orotate/mg RNA incorporation was decreased in the nuclear and microsomal fractions and was increased in the soluble and pH-5 enzyme fractions of the brain of EI and EII groups. Incorporation was also elevated in brain homogenates of EII rats and was reduced in the EI group. It was increased in the mitochondrial fraction of EI animals but did not show any change in the EII group. From these results, it can be concluded that dietary stress during gestation alone (EI) and during growth, gestation, and lactation (EII) modulates the metabolism of nucleic acids and proteins in the whole brain and in various cellular brain fractions.

Keywords: undernourished rats; brain; cellular fractions; RNA; protein; synthesis

Introduction

Prenatal and postnatal dietary restriction exerts a profound effect on the normal functioning of the central nervous system.[1,2] Brain weight, DNA, RNA, and protein content fail to increase normally in young rats subjected to dietary stress.[1,3-5] DNA[6,7], RNA[7,8] and protein synthesis[7-9] also demonstrate variable responses in the brain of undernourished animals. These studies, usually performed on the whole brain of adult animals[7-9] and in the progeny of dietary insulted rats during either gestation[4,10] or growth, gestation, and lactation,[4,10] give very little information on variations of RNA and protein content and their synthesis in various cellular fractions of the brain of well-fed and undernourished rats. The present investigation was undertaken to examine the above-mentioned aspect of the situation.

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Materials and methods

Twenty-four female weanling Sprague-Dawley rats were used. On arrival they were weighed and placed in individual metabolic cages where they received Purina Chow pellets daily. They were weighed regularly and kept under a 12-hour light-dark cycle. The rats were divided into three groups of eight animals each and subjected to the dietary regimes described below. After 15 weeks of growth, they were mated with males of the same strain and checked for vaginal plugs indicating pregnancy.

The first group served as controls. They were fed ad libitum (WF) and received water at will during the experimental period. Food consumption was measured daily for each animal.

The second group (EI) was fed ad libitum during growth and lactation. One week before mating,the animals of this group were subjected to 50% dietary restriction. The quantity of food was determined by calculating the daily food intake of the controls. The dietary restriction continued until the birth of their offspring.

The third group (EII) received 50% of the total diet consumed by the controls during the entire period of growth, gestation, and lactation.

After parturition, eight to ten young were placed with each dam in the WF, EI, and EII groups. Since mortality was significant in the EII group, precautionary measures[4,10] were taken to keep the litter size constant[8,10] during lactation.

Incorporation of radioactivity

After the lactation period, the dams in the three groups were killed by decapitation. Their brains were isolated within 60 seconds and kept in Tris-HCl buffer (pH 7.8) containing 0.25 M sucrose, 0.35 M Tris, 0.4 M $MgCl_2$, 0.025 M KCl and polyvinyl sulfuric acid (1 μg/mL). These organs were dried carefully with cheese cloth, weighed, and placed in 10 volumes of Tris-HCl buffer (pH 7.8) for incubation (1 g of brain in 10 mL of buffer in the presence of 1 μCi of ^{3}H-orotate of 1 μCi of ^{14}C-phenylalanine per mL of buffer) at 37° C for 30 minutes under an atmosphere of humidity-saturated oxygen:CO_2 (95:5).

Cellular fractions

After incubation, the whole mixture was homogenized, and nuclear, mitochondrial, microsomal, and soluble fractions were isolated by differential centrifugation as described elsewhere.[11] A pH-5 enzyme preparation was produced by precipitating the soluble fraction with 1 N acetic acid at pH 5.[12] Various sediments obtained by differential centrifugation and pH-5 precipitation were re-suspended in Tris HCl buffer (pH 7.8) containing 0.035 M Tris, 0.15 M $MgCl_2$ and 0.025 M KCl in the following proportions and homogenized: nuclear and mitochondrial fractions, 1 g tissue per 2 mL of buffer; microsomal fraction, 1 g of tissue per 0.5 mL of buffer; and pH-5 enzyme fraction, 1 g of tissue per 1 mL of buffer.

After measuring the volume of each fraction, 0.2 mL was utilized for radioactivity counts of RNA and protein synthesis; 0.2 mL was employed for the determination of total free amino acids, nucleotides, and nucleic acids; and 25 μL was used for protein measurements as described elsewhere.[10] RNA was assessed by the method of Munro and Fleck[13] and DNA by the diphenylamine reaction as modified by Burton.[14] Protein was measured according to the procedure developed by Goa.[15] Free nucleotide and amino acid content was determined by the respective methodologies described elsewhere by our group.[16,17]

Results

Body weight, organ weight, and DNA content

Table 1 indicates that dietary restriction caused a significant reduction of body weight in EI and EII rats as compared to the WF group. However, this reduction was more pronounced in EII animals. Brain weight did not show any variation in EI rats but decreased in the EII group as compared to the WF controls (*Table 1*). The brain weight:DNA ratio also did not change in EI rats but increased in the EII group in comparison with WF animals (*Table 1*). Brain weight per 100 g body weight rose significantly in EI and EII in relation to WF. DNA content per brain and per g fresh tissue or per 100 g body weight did not change in EI rats (*Table 1*). DNA content per brain and per g fresh tissue was significantly decreased in the EII group but did not vary when expressed per 100 g body weight as compared to WF and EI animals (*Table 1*). No significant differences were noted between EI and WF rats no matter how the results were expressed.

RNA content

The data presented in *Table 2* and *Table 3* show variations of RNA content in various cellular fractions of the brain of WF, EI, and EII rats. In the EI group compared with the WF controls, RNA content per g fresh weight was decreased in microsomes and increased (i) in cytosol when expressed per g fresh weight and per 100 g body weight (*Table 2*) or per mg DNA (*Table 3*); (ii) in nuclei, mitochondria, and pH-5 enzymes when expressed per mg protein (*Table 3*); and (iii) in homogenates, nuclei, and mitochondria when expressed per 100 g body weight.

Table 1 Effect of dietary restriction on the body and brain weight of rats

Group	Body weight (g)	Brain weight (g)			DNA content (mg)	
		/total organ	/100 g body weight	/mg DNA	/organ	/g fresh tissue
WF	355[a] ± 26[b]	1.71 ± 0.03	0.48 ± 0.05	0.58 ± 0.06	2.90 ± 0.35	1.69 ± 0.17
EI	315 ± 21[c]	1.89 ± 0.01	0.60 ± 0.06[d]	0.67 ± 0.07	2.80 ± 0.29	1.55 ± 0.16
EII	267 ± 32[d]	1.63 ± 0.05[d]	0.61 ± 0.06[d]	0.78 ± 0.08[d]	2.10 ± 0.25[d]	1.29 ± 0.13[d]

[a] Each datum is an average of eight animals. The brain weight to DNA ratio represents weight per cell or cell size.
[b] ±S.D.
[c] $P < 0.05$.
[d] $P < 0.01$.

Table 2 RNA content in various cellular fractions of the brain of undernourished rats

Group	Homogenate	Nuclei	Mitochondria	Microsomes	Cytosol	pH-5 Enzyme
			mg/g fresh weight			
WF	2.80[a] ± 0.30[b]	0.54 ± 0.06	0.40 ± 0.05	1.46 ± 0.15	0.31 ± 0.03	0.22 ± 0.03
EI	2.50 ± 0.28	0.54 ± 0.06	0.42 ± 0.05	1.20 ± 0.12[d]	0.40 ± 0.04[d]	0.21 ± 0.03
EII	2.28 ± 0.21[c]	0.54 ± 0.06	0.31 ± 0.03[c]	1.18 ± 0.02[d]	0.26 ± 0.02[d]	0.11 ± 0.02[e]
			mg/100 g body weight			
WF	1.35 ± 0.14	0.26 ± 0.03	0.19 ± 0.02	0.70 ± 0.08	0.15 ± 0.02	0.11 ± 0.01
EI	1.54 ± 0.16[d]	0.32 ± 0.03[d]	0.25 ± 0.03[d]	0.72 ± 0.08	0.24 ± 0.03[d]	0.13 ± 0.01
EII	1.39 ± 0.14	0.33 ± 0.03[d]	0.19 ± 0.02	0.72 ± 0.07	0.16 ± 0.02	0.07 ± 0.08[e]

[a] Each datum is an average of eight animals.
[b] ±S.D.
[c] $P < 0.01$.
[d] $P < 0.05$.
[e] $P < 0.001$.

Table 3 RNA:DNA and RNA:protein ratios in various cellular fractions of the brain of undernourished female rats

Group	Homogenate	Nuclei	Mitochondria	Microsomes	Cytosol	pH-5 Enzyme
			mg RNA/mg DNA			
WF	1.65[a] ± 0.11[b]	0.37 ± 0.03	0.24 ± 0.03	0.85 ± 0.09	0.18 ± 0.02	0.13 ± 0.02
EI	1.73 ± 0.11	0.36 ± 0.04	0.28 ± 0.03	0.81 ± 0.09	0.27 ± 0.03[c]	0.14 ± 0.02
EII	1.77 ± 0.08[c]	0.42 ± 0.04[c]	0.24 ± 0.03	0.92 ± 0.09	0.20 ± 0.03	0.86 ± 0.09[c]
			μg RNA/mg protein			
WF	22.5 ± 2.2	9.30 ± 0.93	12.1 ± 1.2	48.0 ± 5.0	26 ± 3	17 ± 2
EI	22.0 ± 2.3	14.0 ± 1.5[c]	16.0 ± 1.6[c]	41.0 ± 6.0	31 ± 3	23 ± 2[c]
EII	21.5 ± 2.2	10.1 ± 1.1	10.9 ± 1.2	42.0 ± 5.0	42 ± 5[d]	36 ± 4[d]

[a] Each datum is an average of eight animals.
[b] ±S.D.
[c] $P < 0.05$.
[d] $P < 0.001$.

In the brain of EII rats compared with WF controls, RNA content was lower (i) in homogenates, mitochondrial, microsomal, and cytosolar fractions when expressed per g fresh weight (*Table 2*); and (ii) in pH-5 enzyme fractions no matter how the results were expressed (*Tables 2 and 3*). It was increased (i) in homogenates and nuclear fractions when expressed per mg DNA (*Table 3*); (ii) in nuclear fractions when expressed per 100 g body weight (*Table 2*); and (iii) in cytosolar and pH-5 enzyme fractions when expressed per mg protein (*Table 3*).

In the brain of EII rats compared to EI animals, RNA content was lower (i) in homogenates, mitochondrial, cytosolar, and pH-5 enzyme fractions when expressed per g fresh weight and per 100 g body weight (*Table 2*); (ii) in cytosolar and pH-5 enzyme fractions when expressed per mg DNA (*Table 3*); (iii) in nuclei and mitochondria per mg protein (*Table 3*). It was higher (i) in homogenates and nuclei when expressed per mg DNA (*Table 3*); and (ii) in cytosolar and pH-5 enzyme fractions when expressed per mg protein (*Table 3*).

Protein content

Table 4 enumerates the variations of protein content in various cellular fractions of the brain of WF, EI, and EII rats. In the EI group compared with WF controls, protein content was decreased in mitochondrial and pH-5 enzyme fractions when expressed per g fresh weight and in the pH-5 enzyme fraction when expressed per mg DNA. It was increased in microsomes and cytosol when expressed per 100 g body weight and in cytosol when expressed per mg DNA.

In the brain of EII compared to WF controls, protein content was decreased (i) in homogenates, cytosolar, and pH-5 enzyme fractions when expressed per g fresh weight; (ii) in cytosolar and pH-5 enzyme fractions when expressed either per 100 g body weight or per mg DNA. It was increased (i) in microsomes

Table 4 Protein content and protein to DNA ratio in various cellular fractions of the brain of undernourished female rats

Group	Homogenate	Nuclei	Mitochondria	Microsomes	Cytosol	pH-5 Enzyme
			mg/g fresh weight			
WF	124[a] ± 15[b]	58 ± 6	33 ± 4	3.04 ± 0.31	11.70 ± 1.20	12.9 ± 1.4
EI	117 ± 13	52 ± 6	26 ± 3[c]	2.93 ± 0.30	12.71 ± 1.41	9.0 ± 0.9[c]
EII	106 ± 10[c]	53 ± 6	28 ± 3	2.82 ± 0.30	6.12 ± 0.67[d]	3.06 ± 0.32
			mg/100 g body weight			
WF	60 ± 6.2	28 ± 3	16 ± 2	1.46 ± 0.15	5.63 ± 0.57	6.20 ± 0.71
EI	70 ± 80	31 ± 3	16 ± 1.5	1.76 ± 0.16[d]	7.61 ± 0.62[d]	5.39 ± 0.54
EII	64 ± 6.5	32 ± 3	17 ± 2	1.72 ± 0.18[d]	3.74 ± 0.39[d]	1.87 ± 0.2[d]
			mg/mg DNA			
WF	73 ± 8	34 ± 4	20 ± 2	1.79 ± 0.18	6.89 ± 0.71	7.59 ± 0.76
EI	79 ± 8	35 ± 5	18 ± 2	1.98 ± 0.70	8.57 ± 0.80	6.07 ± 0.62[c]
EII	82 ± 9	41 ± 43	22 ± 3	2.19 ± 0.20[c]	4.76 ± 0.51[c]	2.38 ± 0.31[c]

[a] Each datum is an average of eight animals.
[b] ±S.D.
[c] $P < 0.05$.
[d] $P < 0.001$.

Table 5 Total free nucleotides, amino acid content and their specific activities in the brain of undernourished female rats

Group	Absorption at 260 nm (nucleotides) /g fresh weight	/100 g body weight	/mg DNA	Disintegrations per minute × 10^3 /absorption at 260 nm
WF	35.39[a] ± 4.0[b]	17.05 ± 1.91	20.80 ± 2.11	700 ± 60
EI	37.56 ± 3.92	22.53 ± 2.34[c]	25.35 ± 2.18[c]	699 ± 35
EII	35.95 ± 3.75	21.94 ± 2.52[c]	27.90 ± 3.01[c]	768 ± 47
	Absorption at 280 nm (amino acids) /g fresh weight	/100 g body weight	/mg DNA	Disintegrations per minute × 10^3 /absorption at 280 nm
WF	14.78 ± 1.52	7.12 ± 0.73	8.72 ± 0.91	1831 ± 2110
EI	16.49 ± 1.69	9.89 ± 0.11[c]	11.12 ± 1.02[c]	1715 ± 175
EII	12.28 ± 1.13	7.49 ± 0.78	9.52 ± 0.98	2358 ± 125[d]

[a] Each datum is an average of eight animals.
[b] ±S.D.
[c] $P < 0.05$.
[d] $P < 0.001$.

expressed either per 100 g body weight or per mg DNA; and (ii) in nuclei when expressed per mg DNA.

In the brain of EII compared with EI rats, protein content was decreased (i) in homogenates, cytosolar, and pH-5 enzyme fractions expressed per g fresh weight; and (ii) in cytosolar and pH-5 enzyme fractions when expressed either per 100 g body weight or per mg DNA. Protein content was increased in nuclei only when expressed per mg DNA.

Nucleotide and amino acid content and specific activities

Total nucleotide content was augmented when expressed per 100 g body weight or per mg DNA in the brain of EI and EII rats compared with WF controls (*Table 5*). No variations were detected in the brains of EI and EII when expressed per g fresh weight.

Amino acid content was increased when expressed per 100 g body weight and per mg DNA in the brain of EI rats versus the WF group. Amino acid content was diminished when expressed per 100 g body weight and per mg DNA in the brain of EII compared to EI animals.

The specific activity of total nucleotides (*Table 5*) did not reveal any variations between the brains of WF, EI, and EII rats. The specific activity of amino acids did not show any difference between the brains of WF and EI animals but was increased in EII compared to WF and EI rats (*Table 5*).

Table 6 Protein synthesis in various cellular fractions of the brain of undernourished female rats

Group	Homogenate	Nuclei	Mitochondria	Microsomes	Cytosol	pH-5 Enzyme
			dpm/mg protein			
WF	972[a] ± 97[b]	405 ± 43	373 ± 36	293 ± 32	1893 ± 210	451 ± 47
EI	1995 ± 126[c]	517 ± 58[d]	442 ± 13[d]	218 ± 26[c]	2472 ± 251[c]	1931 ± 218[c]
EII	1380 ± 141[c]	485 ± 50[d]	451 ± 91[d]	172 ± 18[c]	2582 ± 291[c]	135 ± 18[c]
			dpm × 10^2 mg RNA			
WF	450 ± 52	432 ± 48	308 ± 33	6.08 ± 0.67	714 ± 81	280 ± 31
EI	672 ± 71[c]	489 ± 53[d]	271 ± 30[d]	6.01 ± 0.61	932 ± 103[d]	810 ± 92[c]
EII	638 ± 68[c]	490 ± 57[d]	418 ± 43[c]	5.38 ± 5.7[d]	1632 ± 172[c]	1360 ± 1141[c]

[a] Each datum is an average of eight animals.
[b] ±S.D.
[c] $P < 0.001$.
[d] $P < 0.05$.

Table 7 RNA synthesis in various cellular fractions of the brain of undernourished female rats

Group	Homogenate	Nuclei	Mitochondria	Microsomes	Cytosol	pH-5 Enzyme
			dpm × 10^2 mg/RNA			
WF	698[a] ± 71[b]	1240 ± 163	523 ± 57	472 ± 46	1732 ± 189	318 ± 35
EI	506 ± 52[c]	628 ± 68[d]	2664 ± 239[d]	289 ± 33[d]	4321 ± 441[d]	907 ± 103[d]
EII	981 ± 93[d]	473 ± 49[d]	550 ± 59	338 ± 39[c]	2921 ± 298[d]	418 ± 43[d]
			dpm × 10^2 mg/DNA			
WF	1155 ± 120	397 ± 42	124 ± 15	405 ± 48	316 ± 36	42 ± 8
EI	876 ± 931	229 ± 31[c]	767 ± 80[d]	235 ± 26[d]	1157 ± 120[d]	129 ± 15[d]
EII	1738 ± 190[d]	198 ± 22[d]	131 ± 15	312 ± 33[c]	584 ± 63[d]	36 ± 4[c]

[a] Each datum is an average of eight animals.
[b] ±S.D.
[c] $P < 0.05$.
[d] $P < 0.001$.

Incorporation of ^{14}C-phenylalanine into proteins (specific activity) and RNA (per ribosomes)

^{14}C-Phenylalanine incorporation was increased in homogenates, nuclear, cytosolar, and pH-5 enzyme fractions when expressed per mg protein or RNA and in mitochondria when expressed per mg protein in the brain of EI versus WF rats (*Table 6*).

Incorporation was decreased (i) in mitochondria when expressed per mg RNA and (ii) in microsomes when expressed per mg protein in the EI group as compared with the WF controls. Incorporation of the radioactive precursor increased (i) in homogenates, nuclei, mitochondria, and cytosol when expressed per mg protein or per mg RNA, and (ii) in the pH-5 enzyme fraction per mg RNA of the brain of EII rats compared to WF animals (*Table 6*). Incorporation was decreased (i) in microsomes when expressed per mg protein or per mg RNA and (ii) in the pH-5 enzyme fraction when expressed per mg protein in the brain of EII versus the WF group.

Incorporation of radioactive phenylalanine was increased when expressed per mg RNA in the mitochondria, cytosol, and the pH-5 enzyme fraction and was decreased (i) in microsomes when expressed per mg protein of RNA; and (ii) in the pH-5 enzyme fraction when expressed per mg protein in the brain of EII rats as compared with EI animals.

Incorporation of ^{3}H-orotate into RNA

^{3}H-Orotate incorporation was decreased in homogenates, nuclei, and microsomes and increased in mitochondria, cytosol, and the pH-5 enzyme fraction when expressed per mg RNA or per mg DNA in the brain of EI compared with WF rats (*Table 7*).

Incorporation was decreased in nuclei and microsomes and increased in homogenates and cytosol when expressed per mg RNA or per mg DNA and in the pH-5 enzyme fraction when expressed per mg RNA in the brain of EII versus WF rats.

^{3}H-Orotate incorporation was increased in homogenates when expressed per mg RNA or DNA and in microsomes per mg DNA. It was decreased in mito-

chondria, cytosol, and the pH-5 enzyme fraction when expressed per mg RNA or DNA and per mg RNA in nuclei of the brain of EII rats compared to the EI group (*Table 7*).

Discussion

Malnutrition has a profound effect on body and organ growth.[8,9] Our results on the low body weight gain in dietary restricted dams (EI and EII) are in close agreement with our previous observations and those of other investigators.[18] The marked influence of malnutrition on brain weight is related to the stage of life at which it is imposed.[4,5,8,19] The results of this study clearly demonstrate that female rats that were undernourished during their entire lifetime had lower brain weight than control animals. These data reveal that food deprivation even after the weanling period has a marked impact on brain growth.[18] It is now well established that malnutrition alters brain development in rats during the first week of life.[1-3] The results of this investigation show that undernutrition modulates various parameters involved in cellular growth of the brain. Malnutrition imposed during gestation (EI) does not modify the DNA content of homogenates of the brain. When comparing the biochemical composition of the brain of rats deprived of food for an entire lifetime (growth, gestation, and lactation, EII) with that of their controls, it is clear that brain DNA is lower in homogenates of the former group. These observations suggest that after the weanling period, brain cells, even though they are dividing at a slow pace, could undergo alterations due to dietary restriction. These results are supported by earlier findings in our laboratory.[18] Undernutrition during EI did not alter in any way the protein and RNA content of brain homogenates. However, mitochondrial, nuclear, and cytosol RNA content was significantly increased in EI dams when expressed in mg/100 g body weight (*Table 2*).

Except for elevations of the RNA:DNA ratio in cytosol and decreases of the protein:DNA ratio in the pH-5 enzyme fraction, we did not notice any change in the RNA:DNA and protein:DNA ratios in homogenates and various cellular fractions of the brain of EI dams. The reduction of RNA and proteins in homogenates and various cellular fractions of EII dams clearly demonstrates that RNA and protein content failed to rise normally in the brain. These results are in close agreement with our earlier observations[4,8] and those of other investigators.[20,21] The brain weight:DNA ratio increased in the homogenate of EII dams, indicating that brain weight does not decrease in a parallel manner in relation to DNA content (*Table 1*), ie, the fall in brain weight was not as low as that of DNA content/organ. These results are very similar to those reported in an earlier study.[8]

Undernourished EI and EII dams had similar quantities of brain nuclear RNA. Cellular messenger RNA is synthesized exclusively in the nucleus. After synthesis, a major portion of the RNA molecule migrates toward the cytoplasm where most of the protein synthesis takes place. According to this hypothesis, the migration of nuclear RNA towards the cytoplasm, a phenomenon that occurs in response to a need for protein synthesis in the cytoplasm, proceeds at a slower pace in older than in younger animals.[11,22]

To explain the reduction of RNA and protein in the brain of undernourished rats, it must be understood that DNA acts as a matrix for RNA synthesis. This reduction of the first cellular constituent (DNA) could decrease RNA synthesis. Similarly, because RNA is necessary for protein synthesis, its diminution will reduce protein synthesis, which could explain in part the decreased protein content in the brain of undernourished rats. This hypothesis is supported by the work of Guglielmone et al.[23] who showed that dietary insult caused a lowering of the specific relative radioactivity of the nuclear, microsomal, and soluble fractions of the brain. However, according to Rosso and Winick,[20] it is difficult to interpret these observations because the same quantity of cellular RNA was found in the brain of control and undernourished rats.

The results presented in this paper clearly indicate increased RNA synthesis in homogenates of the brain of dietary-restricted rats in comparison with the controls. Rosso and Winick[20] demonstrated that the relative specific activity of microsomal RNA of the brain is always lower in undernourished rats between days 10 and 30. Their observations allow us to conclude that the catabolism of cytoplasmic RNA is increased in the brain of malnourished animals. This conclusion is supported by observations of heightened RNAase activity in the brain of malnourished rats[21] and in the liver of protein-restricted rats.[24,25] This increased RNAase activity could intensify RNA degradation and consequently induce a reduction of cerebral RNA[26] parallel to the rapid RNA degradation. Several investigators[27,28] have noted higher protein catabolism in the brain of malnourished rats. These data clearly demonstrate that, in relation to RNA and protein synthesis, catabolism has an edge over anabolism, with the result that cellular constituents, such as RNA and protein, fail to increase normally.

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