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POSTNATAL CHANGES OF BRAIN MONOAMINE LEVELS IN PRENATALLY MALNOURISHED AND CONTROL RATS

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Abstract—The effects of age and prenatal protein malnutrition (6% casein diet) on the concentration of monoamine neurotransmitters and their metabolites and precursors in the hippocampal formation, striatum, brain stem and cerebral cortex were investigated in 1-, 15-, 30-, 45-, 90- and 220-day-old rats. Concentrations of all neurotransmitters, i.e. dopamine, norepinephrine and serotonin, changed significantly during the development. However, two main patterns were recognized. Serotonin in all areas, and dopamine in the striatum, increased from birth to day 45, and declined significantly in 90-day-old rats. In contrast, norepinephrine in all areas, and dopamine in areas other than the striatum, showed the lowest levels in 30-day-old rats, with levels increasing gradually after this age. Concentrations of metabolites paralleled changes in corresponding neurotransmitter levels. Prenatal protein malnutrition did not significantly affect any neurotransmitter concentrations with the exception of increased tryptophan levels (181%) in the hippocampal formation of newborn rats and decreased tyrosine levels (59%) in the striatum of day 30 rats. The results indicate that the monoamine transmitter content varied dynamically throughout postnatal life; however, they seem to counteract the insult from prenatal protein malnutrition after postnatal nutritional rehabilitation. © 1997 ISDN

Key words: malnutrition, development, norepinephrine, dopamine, serotonin.

The central nervous system is extremely vulnerable to environmental perturbations during development, especially during the prenatal and early postnatal period.[19,26] During this stage, neurons extend their axons to the target cells under the direction of specific growth factors(s).[11] Early exposure to toxic chemicals or a diet low in protein, carbohydrates, or calories may result in permanent brain damage in adulthood.[15] Earlier studies have shown that prenatal low-protein malnutrition results in behavioral, neurophysiological, and neurochemical changes.[14]

Malnourished rats have increased resistance to extinction during reversal of food-rewarded alternation task on an elevated T-maze[22] and retarded acquisition of a differential reinforcement of a low-rates operant task.[23] Malnourished rats have a deficit of long-term potentiation,[2] increased inhibition of interneuronally mediated inhibition of excitability of hippocampal granule cells,[1] and delayed development of kindling.[3,4]

Previously, we have found that 220-day-old prenatally protein malnourished rats had a significantly higher basal serotonin (5-HT) release from the hippocampal slices than well-nourished controls.[6] However, hippocampal concentrations of 5-HT, as well as its amino acid precursor l-tryptophan and the metabolite 5-hydroxyindoleacetic acid (5-HIAA), were similar in both groups. The aim of the present study was to assess the impact of prenatal protein malnutrition on levels of monoamine neurotransmitters and their metabolites in different regions of the brain during various postnatal ages.

EXPERIMENTAL PROCEDURES

Animals

The procedure and diet are described elsewhere in detail.[8] Briefly, viral- and antibody-free female rats (Sprague-Dawley, Charles River, MA, U.S.A.; 175–200 g) were provided with a 6 or 25% casein

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diet for 5 weeks prior to mating and until delivery of their offspring. Males (325–350 g) were provided with a 6 or 25% diet for 1 week prior to mating to prepare them for mating which occurred by placing one male with from two to three females on the same diet for one estrous cycle. After mating was confirmed by vaginal smears, pregnant females were caged individually in polycarbonate breeding cages.

Following parturition, all litters were culled to eight pups (four males and four females). Whole culled litters born to mothers with either 6 or 25% casein diets during pregnancy were fostered to control mothers provided with the 25% casein diet who had given birth no more than 36 hr previously. The 25% diet was provided throughout the suckling period. After weaning on day 21, the young rats were housed in groups of two or three with others of the same nutritional history and sex and were fed a standard lab. chow (Purina 5001). The computer-controlled and -monitored animal quarters were maintained at a temperature of $73 \pm 3°F$ with a humidity of 43–74%, and a reverse 12 hr night/12 hr day cycle was maintained throughout to accommodate testing to the waking period of the rat. In this paper, the prenatally malnourished animals are called 6/25 rats and the well-nourished control animals 25/25 rats, to emphasize the diet received prenatally/postnatally.

Tissue preparation

The 6/25 and 25/25 male rats were studied on postnatal days 1 (P1), 15 (P15), 30 (P30), 45 (P45), and 220 (P220) using from five to seven animals per group. Animals were decapitated using a guillotine, and brain tissue was removed immediately. The hippocampal formation, corpus striatum, brain stem, and cerebral cortex were dissected out on ice using the Paxinos and Watson rat atlas.[18] No determination was performed on P1 rats' striatum, brain stem, and cortex, since accurate dissection of these regions was difficult at this age. The dissected tissues were immersed in an ethanol/dry-ice mixture and were kept at $-80°C$ until high-performance liquid chromatographic (HPLC) analysis was performed. Based on previous experience, catecholamines, their metabolites, and amino acids in frozen stored brain were stable up to 3 months. The levels of neurochemicals in the current experiment were analyzed within 1 month.

At the time of HPLC analysis, 1 ml of 0.4 N perchloric acid was added to the brain tissue in an Eppendorf vial and the tissue was sonicated for 20 sec (Bronson, Sonifer 450, Danbury, CT, U.S.A.). The extracts were centrifuged at 12 000 rpm for 15 min (Eppendorf, Centrifuge 5415, Hamburg, Germany) and the supernatants were filtered through a 0.2 μm Rainin syringe filter cartridges. All extraction procedures were performed in a cold room at 4°C. The proteins were quantitated by Lowry's method.[13]

Determination of neurochemical substances

Separation and quantitation of electrochemically active substances were performed by a gradient HPLC with 16-channel coulometric detection (CD) (ESA Inc., Bedford, MA, U.S.A.), as described previously.[5] The sensitivity for detectable neurochemical substances ranged from 50 fmole to 50 pmole. External standards included tyrosine, norepinephrine, 4-methoxy,3-hydroxy-phenyl glycol (MHPG), dopamine, 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), tryptophan, 5-hydroxy-tryptophan, serotonin, and 5-hydroxyindoleacetic acid (5-HIAA). The standards were prepared fresh and were injected into the HPLC–CD system during every five sample runs. Samples from 5/25 and 25/25 rats of the same age were run simultaneously.

Data analysis

All results are expressed as means $\pm$ SD. Two-way ANOVAs, followed by *post hoc* Scheffe' comparisons, were used to analyze the effect of age and nutritional history in each brain area.

RESULTS

Low casein diet given for 5 weeks to female rats prior to mating and until delivery did not affect the pregnancy. As noted previously[22] the prenatally malnourished 6/25 newborn rats showed a 21% body weight deficit at birth compared with 25/25 rats. By weaning, there was still an 11% body

weight deficit in 6/25 vs 25/25 rats. Afterwards, the body weights of two groups were no longer different.

Postnatal changes of neurochemical substances in the hippocampus of 25/25 and 6/25 rats

Table 1 lists the concentrations of ten neurochemical substances from the hippocampus of 25/25 and 6/25 animals at various ages. In both sets of animals, there were substantial differences ($P<0.05$) in the levels of tyrosine, NE, MHPG, DA, HVA, tryptophan, 5-OH-tryptophan, 5-HT, and 5-HIAA at different postnatal ages. The time course of these differences was not the same for all neurotransmitters and their metabolites.

In the dopaminergic and noradrenergic systems, however, the neurotransmitters and their corresponding metabolites exhibited some developmental similarities. Highest levels were present in the suckling pups and the lowest levels in newly weaned rats. For example, the levels of DA and DOPAC increased from P1 to P15 and decreased at P30. From P30, the DA level increased continuously until P220, while DOPAC and HVA levels remained relatively low. The NE levels also were lowest in P30 rats and began to increase gradually later, while MHPG maintained a relatively constant level throughout the postnatal development. Tyrosine levels were high at both P1 and P15, decreased at P30, and then gradually increased.

In the serotoninergic system, the 5-HT and 5-HIAA remained unchanged between P1 and P30 and increased significantly at P45, decreased at P90, and increased again at P220. The immediate precursor of 5-HT, 5-OH-tryptophan, remained at a low level until P90, and then increased at P220. Conversely, tryptophan levels were high at P1 and decreased thereafter.

Comparing the 25/25 and 6/25 rats, neurochemical levels at all ages were similar. The only significant difference was in the tryptophan level, which was two-fold higher in P1 malnourished rats than in controls. There were no significant interactions between the age and nutritional status for all substances measured in this study (data not shown).

Postnatal changes of neurochemical substances in the striatum of 25/25 and 6/25 rats

As shown in Table 2, there were significant differences ($P<0.05$) in the levels of all 10 neurochemical substances at various postnatal ages, ranging from P15 to P90. The ontogenetic changes of the levels of 5-HT, 5-HIAA, NE, and their amino acid precursors, tyrosine and tryptophan, showed a very similar pattern to that displayed in the hippocampus. In the dopaminergic system,

Table 1. Concentrations of neurochemical substances in hippocampal formation of control (C) and prenatally malnourished (M) rats*†

Compound	Group	Age (days) 1	15	30	45	90	220	*F* value
Tyrosine‡	C	588.52±145.5	535.02±69.63	58.99±4.82	148.05±11.72	233.06±23.76	297.78±15.15	186.08
	M	569.34±273.1	480.35±80.31	79.89±19.46	122.46±2.74	180.58±4.59	301.10±7.85	3.32
Norepinephrine‡	C	0.40±0.18	0.93±0.23	0.40±0.03	1.46±0.21	2.99±0.26	6.53±0.27	285.25
	M	0.53±0.10	1.25±0.42	0.65±0.14	1.12±0.08	2.81±0.12	7.21±0.08	0.93
MHPG‡	C	0.31±0.05	0.30±0.07	0.17±0.10	0.22±0.02	N.D.	0.20±0.03	5.77
	M	0.42±0.14	0.56±0.44	0.05±0.01	0.17±0.01	N.D.	0.21±0.02	0.23
Dopamine‡	C	0.74±0.78	2.21±3.96	0.08±0.04	0.09±0.03	0.17±0.01	0.35±0.03	2.80
	M	1.02±0.75	1.69±2.99	0.04±0.01	0.04±0.01	0.16±0.02	0.48±0.11	0.05
DOPAC	C	0.89±0.92	2.36±4.05	N.D.	0.25±0.07	0.27±0.04	0.20±0.04	2.65
	M	0.96±0.61	1.13±1.14	N.D.	0.14±0.03	0.88±0.26	0.16±0.02	0.23
HVA‡	C	1.39±0.83	1.67±2.49	0.05±0.02	0.25±0.06	0.13±0.02	0.23±0.05	4.66
	M	2.01±1.05	1.07±0.90	0.04±0.01	0.16±0.03	0.19±0.03	0.20±0.03	0.39
Tryptophan‡	C	286.87±116.6	51.65±11.82	N.D.	48.18±3.63	39.28±17.57	12.44±0.75	265.77
	M§	518.29±186.4	56.60±13.65	N.D.	40.50±1.40	36.62±16.38	13.01±0.53	4.69
5-OH-Tryptophan‡	C	0.11±0.06	0.11±0.09	N.D.	0.09±0.02	0.12±0.01	0.24±0.03	14.84
	M	0.13±0.08	0.12±0.02	N.D.	0.08±0.01	0.15±0.02	0.19±0.02	0.18
Serotonin‡	C	0.62±0.29	0.49±0.13	1.00±0.07	5.98±1.71	0.93±0.42	12.54±1.75	91.11
	M	0.37±0.19	0.79±0.26	1.51±0.40	3.14±0.55	1.46±0.65	13.23±0.43	0.29
5-HIAA‡	C	2.71±0.80	2.62±0.73	1.43±0.10	8.4±0.64	1.57±0.13	12.32±1.09	149.02
	M	2.81±1.31	2.97±0.88	1.82±0.35	6.5±0.22	1.76±0.12	12.46±0.92	0.16

*Concentrations are expressed as ng/mg of protein and numbers are means of from five to seven determinations ± SD.

†Abbreviations: MHPG, 4-methoxy,3-hydroxy-phenylglycol; DOPAC, 3,4-dihydroxyphenylacetic acid; HVA, homovanillic acid; 5-HIAA, 5-hydroxyindoleacetic acid; N. D., not determined.

‡$P<0.05$ for difference due to age.

§$P=0.02$ for difference due to malnutrition.

‖*F* value on the top line of each chemical due to age effect; bottom line due to malnutrition effect.

Table 2. Concentrations of neurochemical substances in the striatum of control (C) and malnourished (M) rats*†

Compound	Group	Age (days) 15	30	45	90	*F* value‖
Tyrosine‡	C	575.23±79.95	61.40±18.05	175.60±14.17	193.11±11.30	108.77
	M§	495.47±130.71	36.46±6.13	122.86±11.51	185.26±25.14	5.03
Norepinephrine‡	C	0.59±0.26	0.17±0.04	0.38±0.02	0.74±0.05	9.28
	M	0.68±0.28	0.18±0.04	0.50±0.01	0.68±0.16	0.37
MHPG‡	C	0.40±0.08	N.D.	0.70±0.09	<0.28	7.98
	M	0.50±0.17	N.D.	0.37±0.10	<0.28	2.91
Dopamine‡	C	9.19±4.73	13.14±3.72	18.60±1.97	12.70±4.97	3.96
	M	7.26±4.26	7.06±1.16	14.64±1.16	11.39±4.61	2.00
DOPAC‡	C	13.47±4.94	20.33±7.50	29.22±3.65	27.43±4.48	10.45
	M	12.99±7.53	11.67±4.16	20.36±4.17	40.78±4.13	0.00
HVA‡	C	6.75±3.80	3.07±0.42	14.16±1.01	9.65±0.60	17.60
	M	8.12±4.16	1.65±0.29	9.49±1.44	10.47±0.87	2.01
Tryptophan‡	C	56.35±12.07	N.D.	63.55±3.99	82.77±5.30	13.62
	M	60.71±8.78	N.D.	43.09±6.15	82.37±9.22	2.05
5-OH-Tryptophan‡	C	1.18±1.91	N.D.	0.15±0.02	0.83±0.08	7.39
	M	0.27±0.13	N.D.	0.09±0.01	1.10±0.18	0.67
Serotonin‡	C	0.42±0.12	1.26±0.30	3.14±0.30	0.78±0.09	48.97
	M	0.43±0.15	0.93±0.21	2.71±0.41	0.36±0.06	2.99
5-HIAA‡	C	2.54±0.34	1.72±0.29	9.46±0.77	2.07±0.15	46.98
	M	2.80±1.38	1.25±0.21	6.73±1.12	2.10±0.17	3.60

*Concentrations are expressed as ng/mg of protein and numbers are means of from five to seven determinations ± SD.
†Abbreviations: see Table 1.
‡$P<0.05$ for difference due to age.
§$P<0.05$ for difference due to malnutrition.
‖*F* value on the top line of each chemical due to age effect; bottom line due to malnutrition effect.

DA and DOPAC increased gradually from P15 to P45, with a subsequent decrease at P90. The HVA level decreased from P15 to P30 but increased significantly at P45 with subsequent decrease at P90. In the serotoninergic system, although 5-HT and 5-HIAA followed a trend similar to that observed in the hippocampus, the 5-OH-tryptophan was lowest at P30 and P45, while regaining its P15 level by P90.

Prenatal protein malnutrition had a significant impact only on the level of tyrosine which was significantly lower in malnourished rats than in controls. There were no significant interactions between the age and nutritional status for all substances measured in this study (data not shown).

Postnatal changes of neurochemical substances in the brainstem of 25/25 and 6/25 rats

Similar to the results shown in the hippocampus and the striatum, significant age differences ($P<0.05$) in levels of nine neurochemical substances (except MHPG) were observed in the brain stems of both sets of animals (Table 3). Levels of tyrosine, NE, 5-HT, and 5-HIAA from P15 to P90 exhibited developmental patterns very similar to those observed in the hippocampus and striatum. In the dopaminergic system, DA, DOPAC, and HVA decreased at P30; however, the neurochemicals either recovered (DA and DOPAC) or returned (HVA) close to their P15 levels at P90. The level of 5-OH-tryptophan showed a constant increase from P15 to P90, and tryptophan levels were also highest at P90.

Prenatal protein malnutrition did not have any effect on the content of neurochemicals in the brain stem. There were no significant interactions between the age and nutritional status for all substances measured in this study (data not shown).

Postnatal changes of neurochemical substances in the cortex of 25/25 and 6/25 rats

Consistent with the other areas of the brain, there were age-related significant differences ($P<0.05$) in the levels of all 10 neurochemical substances in the cortex (Table 4). The levels of tyrosine, NE, MHPG, tryptophan, 5-HT, and 5-HIAA exhibited very similar ontogenetic changes to those observed in the hippocampus. Levels of DA, DOPAC, and HVA decreased from P15 to P30, followed by an increase at P45. At P90, DA and DOPAC levels increased further, while HVA

Table 3. Concentrations of neurochemical substances in the brain stem or control (C) and malnourished (M) rats*†

Compound	Group	Age (days) 15	30	45	90	F value§
Tyrosine‡	C	451.63±63.31	78.04±17.74	107.48±5.35	348.25±16.66	119.93
	M	361.92±70.34	102.87±11.74	92.49±5.92	365.03±27.30	0.93
Norepinephrine‡	C	2.67±0.48	1.57±0.30	2.60±0.12	4.20±0.33	32.17
	M	2.53±1.01	1.59±0.30	2.59±0.25	4.96±0.40	0.83
MHPG	C	0.18±0.08	N.D.	0.15±0.02	0.14±0.02	0.93
	M	0.16±0.07	N.D.	0.13±0.14	0.16±0.02	0.00
Dopamine‡	C	3.39±1.84	0.61±0.09	1.07±0.23	3.02±1.27	6.81
	M	3.52±1.42	0.94±0.18	1.44±0.28	2.12±0.34	0.02
DOPAC‡	C	1.84±1.06	0.03±0.01	1.04±0.22	2.72±0.37	24.70
	M	1.78±0.51	0.04±0.01	1.65±0.33	3.32±0.46	1.85
HVA‡	C	1.70±0.87	0.21±0.04	0.74±0.13	0.72±0.11	16.48
	M	1.60±0.48	0.54±0.20	1.03±0.21	0.74±0.09	0.85
Tryptophan‡	C	38.64±7.37	N.D.	35.67±1.49	57.53±2.61	37.68
	M	40.29±9.12	N.D.	37.23±1.95	67.47±4.96	3.13
5-OH-Tryptophan‡	C	0.11±0.14	N.D.	0.18±0.01	0.43±0.05	26.87
	M	0.09±0.05	N.D.	0.14±0.01	0.69±0.13	2.35
Serotonin‡	C	1.68±0.41	3.90±0.62	8.11±0.26	2.37±0.43	79.11
	M	1.74±0.64	3.71±0.67	8.26±0.85	2.23±0.20	0.01
5-HIAA‡	C	6.44±1.93	3.64±0.78	8.52±0.62	2.09±0.16	45.71
	M	5.13±1.68	3.90±0.60	7.62±0.31	2.81±0.30	0.40

*Concentrations are expressed as ng/mg of protein and numbers are means of from five to seven determinations±SD.
†Abbreviations: see Table 1.
‡$P<0.05$ for difference due to age.
§F value on the top line of each chemical due to age effect; bottom line due to malnutrition effect.

remained unchanged. The 5-OH-tryptophan levels were very low and were measurable only at two ages.

The prenatal protein malnutrition did not change the levels of neurochemical substances in the cerebral cortex. There were no significant interactions between the age and nutritional status for all substances measured in this study (data not shown).

Table 4. Concentrations of neurochemical substances in the cortex of control (C) and malnourished (M) rats*†

Compound	Group	Age (days) 15	30	45	90	F value§
Tyrosine‡	C	507.36±68.42	77.53±6.60	115.49±3.50	168.56±7.41	174.83
	M	412.00±86.58	97.75±13.52	104.52±3.71	148.83±5.96	3.98
Norepinephrine‡	C	0.75±0.13	0.61±0.11	0.65±0.10	2.00±0.14	57.68
	M	0.80±0.20	0.86±0.17	0.84±0.20	1.94±0.09	0.87
MHPG‡	C	0.17±0.02	N.D.	0.20±0.02	0.12±0.01	20.90
	M	0.17±0.04	N.D.	0.17±0.02	0.12±0.01	0.56
Dopamine‡	C	1.81±0.46	1.10±0.38	1.13±0.54	5.31±0.95	13.16
	M	2.27±1.72	1.02±0.29	1.13±0.38	4.81±0.55	0.01
Dopac‡	C	0.97±0.26	0.02±0.01	0.65±0.20	1.93±0.21	53.48
	M	0.91±0.29	0.01±0.00	0.70±0.17	2.60±0.21	3.17
HVA‡	C	1.24±0.09	0.44±0.14	0.98±0.24	0.79±0.07	15.65
	M	1.22±0.21	0.48±0.14	0.91±0.11	0.84±0.04	0.01
Tryptophan‡	C	31.22±3.92	N.D.	31.57±1.93	39.04±2.07	7.12
	M	35.32±5.44	N.D.	35.45±1.07	39.32±1.24	2.43
5-OH-Tryptophan‡	C	0.03±0.01	N.D.	N.D.	0.13±0.02	55.95
	M	0.03±0.01	N.D.	N.D.	0.19±0.02	3.78
Serotonin‡	C	0.03±0.02	1.73±0.22	3.23±1.05	0.94±0.08	25.94
	M	0.07±0.04	1.93±0.23	2.95±0.31	0.88±0.05	0.01
5-HIAA‡	C	0.10±0.03	1.75±0.27	4.58±0.58	1.06±0.07	120.66
	M	0.11±0.03	2.11±0.29	4.22±0.28	1.15±0.02	0.06

*Concentrations are expressed as ng/mg of protein and numbers are means of from five to seven determinations±SD.
†Abbreviations: see Table 1.
‡$P<0.05$ for difference due to age.
§F value on the top line of each chemical due to age effect; bottom line due to malnutrition effect.

DISCUSSION

The present data summarize our neurochemical analysis of the changes in contents of neurotransmitters and metabolites during postnatal development under two nutritional conditions. The results indicate that there are dramatic changes in serotoninergic, dopaminergic, and noradrenergic transmitters and their metabolites in several brain regions during ontogenetic development, especially during the post-weaning period. However, the results also indicate that prenatal protein malnutrition, followed by postnatal rehabilitation, did not have a significant effect on the levels of neurotransmitters and their metabolites. Since the main focus of current study is to correlate the effect of prenatal protein malnutrition on the development of neurotransmitter systems with previously found enhanced hippocampal 5-HT release at P220, only hippocampal tissues were analyzed completely through this time point.

We have found two main patterns of neurochemical changes with age. The first one was exhibited by 5-HT in all brain areas and by dopamine in the striatum. These levels increased from birth to 45 days of age, with subsequent decrease at 90 days. The increase in 5-HT and 5-HIAA at P45 may suggest an enhanced synaptogenesis or synthesis that occurred in 5-HT terminals during this period. Anatomical data did reveal a significant effect of age on synaptic spine density of the dentate granule cells during this developmental period, i. e. the number increased from P15 to P30, dropped at P90, and increased again at P220.[7] However, the localization of the serotoninergic synapses in the hippocampus is unclear since the layer of granule cells is almost completely devoid of 5-HT innervation.[24]

The second pattern of neurochemical changes was exhibited by norepinephrine in all areas and by dopamine in all areas except for the striatum. Concentrations of NE in the hippocampal formation increased from P1 to P15, but were the lowest in all areas at P30 followed by a gradual increase. This could indicate a lower neuronal activity after weaning than during early noradrenergic development. The NE levels were reported to increase gradually from embryonic day 15 (E15) until postnatal day 30 (P30).[9,10,17] However, the ratio of MHPG over NE+epinephrine did drop dramatically from P1 to P80 in the whole brain.[10]

This second pattern was also exhibited by hippocampal DA, DOPAC, and HVA levels which increased from P1 to P15, with a decrease at P30, and gradual increase later. The decrease during the post-weaning period was also present in the brainstem and cortex and may reflect a general decrease of neuronal activation of the mesolimbicortical DAergic pathway during this critical developmental stage. Developmental changes in the DA content in the midbrain and frontal cortex were reported, with a sharp increase in DA occurring during postnatal week 3, followed by an equally sharp decline at P30, and a subsequent gradual increase through adulthood.[16] On the other hand, other investigators found that the levels of mesencephalic and diencephalic DA increase sharply after birth and rise continuously to attain the adult state around P30.[9,17]

The nigrostriatal DA system changed during development with a pattern similar to that of 5-HT. Both DA and DOPAC levels in the striatum reached their highest levels at P45 and decreased by P90. HVA levels decreased from P15 to P30 but also were highest at P45 with subsequent decline. This ontogenic pattern for DA in the striatum was reported previously, with both the D_2 receptor number and DA content increasing after birth, reaching a maximal level at P30, and decreasing by approximately 40% in adult ages.[16] Thus, two major DAergic systems in the brain have different developmental patterns.

A number of previous investigators have found effects of malnutrition on neurotransmitter levels;[12,20,21,26] however, they are in disagreement about the magnitude of the changes and/or whether the changes could be completely reversed after nutritional rehabilitation. In addition to the differences in the composition of diets, timing of nutritional insult, and parental–offspring environments, there are other variables, such as different brain regions and methods of measurement that make comparison difficult. In the present study, we did not find any significant differences between neurotransmitter levels in four brain areas of control and malnourished rats.

In conclusion, although morphologically the brain's monoamine pathways are well developed in the late gestation and early postnatal stages in the rats, their neurotransmitter content varied throughout postnatal life. Prenatal protein malnutrition did not change concentrations of monoamine neurotransmitters, although it does affect some functional parameters, such as serotonin[6] and dopamine release.[25]

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