ANALYSIS OF THE ROLE OF ADRENERGIC BRAIN STRUCTURES IN THE GENESIS OF GROWTH RETARDATION

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UDC 612.65-06:612.822.2

The catecholamine (CA) content in the brain and adrenals of physiologically mature and immature rats aged 1-30 days was compared with changes in the weight of the whole body, brain, and adrenals and with certain indices of development. The CA content in the brain and adrenals of physiologically immature animals was much lower than in mature rats; there was a corresponding delay in growth of the whole body, the brain, and the adrenals. The heart rate in the physiologically immature animals was reduced and the time of acquiring vision and cutting of the teeth was delayed. The role of CA in the genesis of retardation of growth in physiologically immature rats in the postnatal period is confirmed by the lower rate of growth of the whole body and brain and by the increase in their CA content.

Physiologically mature animals whose physiological age corresponds to their calendar age are characterized in early postnatal development by a high level of oxygen consumption and high activity of their respiratory and cardiovascular systems [2]. A contributory factor to these features is the earlier onset of the functioning and the predominantly sympathico-adrenergic character of the mechanisms of regulation, and it produces a high growth constant at an early age [6]. Catecholamines (CA) are known to increase O_2 consumption, especially at an early age [9], and to activate various enzymes and metabolic processes [7, 10]. Physiological immaturity, defined as disparity between the physiological and calendar ages [2], is characterized by retardation of growth and development and by a decrease in energy expenditure and in the level of activity of the autonomic systems [1, 8]. In previous research in the author's laboratory, physiological immaturity was induced by administration of adrenergic blocking drugs [3, 5, 6].

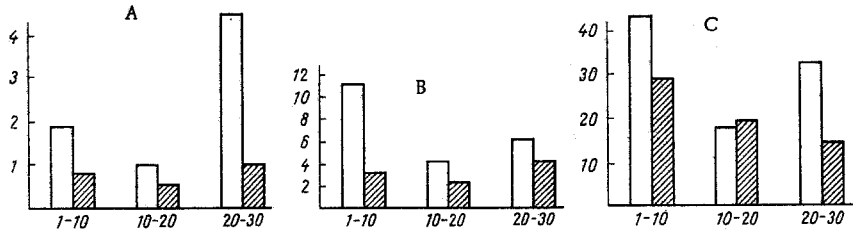

Fig. 1. Rate of change of body weight and of increase in CA content in brain and adrenals of physiologically mature (unshaded columns) and immature (shaded columns) rats. Abscissa: age periods (in days); ordinate: A) rate of increase of body weight (in g/day); B) rate of increase of CA content in brain (in μg/g tissue/day); C) rate of increase of CA content in adrenals (in μg/g tissue/day).

Laboratory of Age Physiology and Pathology, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 3, pp. 23-26, March, 1974. Original article submitted May 10, 1973.

TABLE 1. Indices of Development and Catecholamine Content in the Brain and Adrenals of Physiologically Mature and Immature Rats (M ± m)

Group of rats	Index studied	Time after birth (in days)						
		1	5	7	10	20	25	30
Mature	Body wt. (in g)	6,2±0,17	12,4±0,24	19,0±0,4	24,9±0,5	35,0±0,4	60,0±0,4	80,4±1,24
Immature		4,0±0,09	7,28±0,07	9,78±0,05	12,6±0,19	18,5±0,46	25,0±0,45	28,8±0,8
	P	<0,001	<0,01	<0,001	<0,001	<0,01	<0,01	<0,01
Mature	Wt. of brain (in g)	0,260±0,06	0,550±0,007	0,650±0,08	0,800±0,01	1,190±0,08	1,240±0,01	1,300±0,01
Immature		0,225±0,001	0,380±0,009	0,431±0,005	0,570±0,004	0,829±0,009	0,900±0,005	1,010±0,008
	P	<0,001	<0,01	<0,001	>0,5	<0,001	<0,02	<0,001
Mature	NA content in brain (in µg/g wet tissue)	0,09±0,001	0,13±0,005	0,16±0,001	0,20±0,01	0,24±0,01	0,27±0,007	0,30±0,002
Immature		0,06±0,02	0,07±0,02	0,08±0,02	0,09±0,02	0,11±0,03	0,119±0,03	0,15±0,003
	P	>0,5	<0,01	0,001	<0,1	<0,01	<0,01	<0,001
Mature	Wt. of adrenals (in mg)	1,5±0,006	2,46±0,13	2,66±0,13	3,83±0,06	7,5±0,05	10,0±1,3	12,5±0,2
Immature		1,0±0,30	2,17±0,60	2,50±0,70	3,00±0,90	6,20±0,90	7,5±0,13	8,3±1,4
	P	>0,1	>0,1	>0,1	>0,1	>0,1	>0,5	<0,001
Mature	CA content in adrenals (in µg/g wet tissue)	485±6,4	600±5,8	701±7,0	920±14,9	1098±10,8	1200±30	1400±20,2
Immature		416±6,0	500±7,5	602±12,5	710±19,4	899±21,3	1010±38	1040±42
	P	<0,001	<0,001	<0,001	<0,001	<0,001	<0,001	<0,001
Mature	Heart rate per minute	288±6,5	390±7,5		407±5,3	460±15,3	—	490±8,2
Immature		267±5,1	360±7,7		380±3,2	420±6,0	—	460±3,0
	P	<0,001	>0,5	—	<0,001	>0,1	—	<0,001

In the investigation described below, the relationship between rates of growth and development and the CA content in the brain and adrenals was studied in rats whose physiological maturity or immaturity was determined at birth.

EXPERIMENTAL METHOD

Experiments were carried out on 175 physiologically mature and immature rats during the first month of life. The body weight of the physiologically mature newborn animals was 6.2 ± 0.17 g, their body temperature 32.3 ± 0.12°, and their heart rate 288.0 ± 6.5/min. The corresponding parameters of the physiologically immature rats were 4.0 ± 0.09 g, 29.3 ± 0.4°C, and 267.0 ± 5.0/min ($P < 0.01$). On the 1st, 5th, 7th, 10th, 20th, 25th, and 30th days of life in both groups of animals the noradrenalin (NA) content in the brain and the total content of NA and adrenalin (A) in the adrenals were determined fluorimetrically and changes in the weight of the whole body, brain, and adrenals, the times of acquisition of sight and cutting of the teeth, and the heart rate judged from the ECG, were investigated. At each of the above times 15 physiologically mature and 10 immature rats were decapitated.

EXPERIMENTAL RESULTS AND DISCUSSION

The results are given in Table 1. The rate of increase of body weight of the mature rats between the 1st and 10th days was much higher than between the 10th and 20th days. There was a correspondingly sharper increase in the CA content in the brain and adrenals during the first 10 days of life and a subsequent slowing of the increase between the 10th and 20th days. From the 20th to the 30th day there was a fresh sharp increase in body weight accompanied by a second considerable increase in the CA content in the brain and adrenals. Periods of acceleration or slowing of gain in body weight of physiologically mature rats thus correspond to acceleration or slowing of the increase in the CA content in the brain and adrenals.

In the physiologically immature rats the initial deficit of body weight compared with the mature animals increased with age. The brain of the immature rats also increased in weight much more slowly. Throughout the period of the experiment these reduced rates of growth of the whole body and brain corresponded to lower NA concentrations in the brain than in the mature rats. There was a very close resemblance between the slower rate of increase of the NA level in the brain, on the one hand, and of the body weight on the other hand, in the physiologically immature rats.

The weight of the adrenals and their CA content also were lower in the physiologically immature than in the mature rats.

To compare the dynamics of growth and of the CA content in the brain and adrenals, the rate of change of body weight (in g/day) and the rate of increase of CA in the organs (in μg/g tissue/day) were calculated for the 1st, 2nd, and 3rd 10-day periods after birth (Fig. 1). The rates of rise of these indices in the physiologically mature rats were higher at all stages of development than in the immature rats.

The physiologically immature rats with delayed growth were characterized by delayed developments as reflected in several indices: cutting of the teeth and development of sight occurred 2 days later in these animals; their heart rate was lower than that of the mature rats (Table 1). The heart of the physiologically mature rats reached a maximum (520 ± 4.7/min) on the 35th day, but not until the 45th day in the immature rats (510.0 ± 8.3/min).

The lowered indices of development of the physiologically immature rats during the first month of life were thus accompanied by a correspondingly reduced CA content in the brain and adrenals.

These observations confirm the view that adrenergic mechanisms of regulation are concerned with the establishment of normal rates of growth and development in the early postnatal period and also on the role of CA deficiency in the genesis of retarded growth and of physiological immaturity.

By activating the enzyme adenyl cyclase, catecholamines increase the conversion of ATP into 3',5'-AMP, an activator of phosphorylase and other enzymes [11]. In connection with the increase in adenyl cyclase activity in the brain of rat during the first month of life [10, 12], it can be postulated that the observed correlation between changes in the CA content and the rate of development may be connected with the influence of CA on metabolic processes.

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