ADRENERGIC MECHANISMS OF REGULATION OF MOTOR RESPONSE IN EARLY POSTNATAL RATS

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Significantly more motor responses (MR) of twitch type during sleep are observed in rats during the first days of life than in adult animals [3]. Cholinergic and GABA-ergic mechanisms of MR regulation were demonstrated previously in rats during early postnatal development [4]. It was decided to study the role of the catecholaminergic system in the regulation of movements of twitch type since the catecholamine concentration in the blood is substantially higher in the early postnatal period than in adult animals [2, 5].

The aim of this investigation was to study the role of adrenergic mediators as a factor in neurohumoral regulation of MR of twitch type in rats in the early postnatal period.

EXPERIMENTAL METHOD

The action of the pharmacologic agents L-dopa, reserpine, and chlorpromazine on the character of performance of MR of twitch type in rats 12 days old was analyzed. The action of chlorpromazine on performance of MR throughout the 1st month of life also was analyzed. The aim was to assess the action of the drug at critical periods of growth. The intensity of growth is known to differ at different ages during early postnatal development: A relatively slow rate of growth is followed by a critical increase [3]. MR were recorded by means of piezocrystals mounted in the floor of transparent plastic cages. MR (actogram) was analyzed by ÉÉGP4-02 electroencephalograph and recorded on an oscilloscope, and also by means of an electronic integrator, constructed according to a scheme described previously [1]. The cages were heated with an electric lamp to 25°C. At that temperature the rats quickly fell asleep and they began to exhibit MR of twitch type. The rats in the experiments of series I received an intraperitoneal injection of L-dopa, a precursor for catecholamine synthesis (10 mg/kg), those in series II received the adrenolytic drug reserpine (0.5 mg/kg), which promotes catecholamine release from the tissues [6], and in series III they received chlorpromazine, an α-adrenoblocker and antagonist of dopamine receptors (10 mg/kg). The drugs for study were dissolved in isotonic solution and injected intraperitoneally in a volume of 0.1-0.2 ml. The initial frequency of MR was recorded first, followed by their frequency after injection of the isotonic solution, immediately after injection of the drug, and 30 min later. The rate of growth of the animals was estimated as the growth rate constant, by the equation [3]:

$$K = \frac{\log m_1 - \log m_2}{\log t_1 - \log t_2},$$

where m_1 and m_2 denote the weight of the animals and t_1 and t_2 their age. The rats were weighed daily in the morning. In the first three series 46 rats were used. In the last series, the action of chlorpromazine in a dose of 10 mg/kg on the character and frequency of MR in the animals was studied.

EXPERIMENTAL RESULTS

L-dopa caused an increase in frequency of MR of twitch type in rats 12 days old from 638 ± 48 to 691 ± 36 per hour ($P < 0.05$, Fig. 1a). After injection of reserpine the frequency of MR fell from 628 ± 56 to 434 ± 31 per hour ($P < 0.001$, Fig. 1b). Chlorpromazine had the same effect in 12-day-old rats on the frequency of MR of twitch type as reserpine, reducing it from 631 ± 39 to 523 ± 19 ($P < 0.05$, Fig. 1c).

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TABLE 1. Frequency of Motor Responses (FMR) of Twitch Type before (A) and after (B) Injection of Chlorpromazine (10 mg/kg), Relative Decrease (RD) of FMR after Injection of Chlorpromazine, Weight Characteristics (weight in grams), and Growth Rate Constant (K) in Rats during 1st Month of Postnatal Development

Parameter studied	Age of animals, days											
	1		2		5		7		9		11	
	A	B	A	B	A	B	A	B	A	B	A	B
FMR ($M \pm m$)	—	—	374±51	152±24	626±64	288±31	647±66	309±30	832±59	565±29	623±85	478±32
RD, %	—	—	59,5		54,1		52,3		34,2		23,4	
Weight in grams, ($M \pm m$)	6,1±0,1		6,9±0,1		8,7±0,22		12,3±0,34		15,2±0,4		16,8±0,4	
K	—		0,48		0,86		0,98		1,3		0,91	

(continued)

Age of animals, days												
13		16		18		23		25		28		30	
A	B	A	B	A	B	A	B	A	B	A	B	A	B
285±46	478±23	85±22	29±7,8	132±12	34±5,6	163±14	60±8,4	349±21	229±18	88±9	57±6,3	76±8	42±6,8
38,4		65,9		74,4		64,9		34,4		35,6		44,8	
18,2±0,62		20,9±0,61		22,4±0,9		30,2±0,96		43,4±0,72		45,8±0,84		46,8±0,84	
0,48		0,39		0,38		3,31		4,31		0,42		0,36	

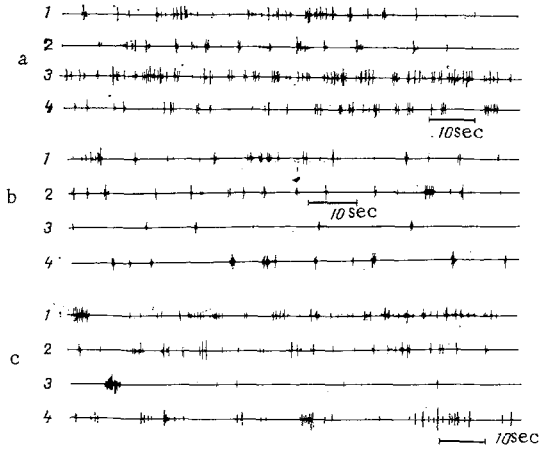

Fig. 1

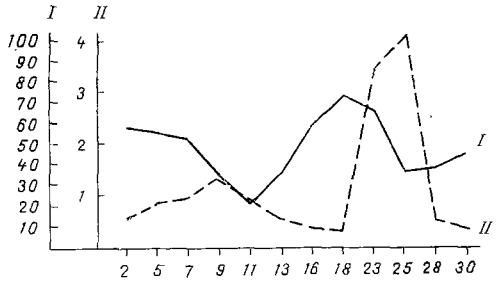

Fig. 2

Fig. 1. Actogram of MR of twitch type performed by rats aged 12 days after receiving L-dopa (a), reserpine (b), and chlorpromazine (c). 1) Original actogram, 2) after injection of isotonic solution, 3) after injection of drug, 4) 30 min after injection of drug.

Fig. 2. Changes in frequency of MR of twitch type after injection of chlorpromazine (10 mg/kg) into rats during 1st month of life, in relation to changes in the character of their growth. Ordinate, age of rats (in days). I) Change in frequency of MR (in %); II) growth rate constant.

It will be clear from Table 1 and Fig. 2 that there were two jumps in growth of the rats: at the ages of 9-11 days and 25-27 days. It was shown previously that during a jump in growth there is an increase in frequency of MR of twitch type [3]. During a jump of growth there was a decrease in the percentage of change in the frequency of MR in response to injection of the same dose of chlorpromazine into the animals. In other words, the same dose of chlorpromazine led to dissimilar changes expressed as a decrease in frequency of MR. During jumps of growth these changes diminished critically.

L-Dopa, which increases the dopamine concentration, thus caused an increase in frequency of MR of twitch type in rats in the early postnatal period. Conversely, reserpine (adrenolytic agent) and chlorpromazine (α-adrenoblocker and antagonist of dopamine receptors) reduced the frequency of MR. The high frequency of MR

of twitch type in the early postnatal period in rats is the result not only of the characteristics of cholinergic and GABA-ergic regulation, as was observed in a previous investigation [4], but also of the high activity of the adrenergic (dopaminergic) system, as the present investigation showed. In addition, it was found that chlorpromazine, in the same dose per kilogram body weight but at different age periods, induces varied changes in the reduction of MR frequency: During jumps of growth there is a maximal increase in the blood catecholamine concentration, so that a larger dose of the drug was evidently needed to produce an equal (expressed as a percentage) decrease in the frequency of MR. A high blood level of catecholamines during this period is confirmed by data in the literature [2, 5].

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CONTENT OF ANTIDIURETIC HORMONE IN THE ADULT ALBINO RAT NEUROHYPOPHYSIS AFTER INJECTION OF HYDROCORTISONE IN THE EARLY POSTNATAL PERIOD

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Critical periods in postnatal development of the system for water and electrolyte homeostasis are known to exist in mammals [3]. The writers showed previously that if hydrocortisone is administered in the neonatal period, the osmotic concentration function in the kidney in adult rats can be substantially modified [2]. The period of sensitivity to this procedure is limited to the age interval from 5 to 9 days after birth [10]. Low antidiuretic reactivity in rats induced in early ontogeny is evidently the result of modification of the molecular mechanisms responsible for sensitivity of the renal epithelium to antidiuretic hormone (ADH). Meanwhile the possibility cannot be ruled out that definite changes could also take place at the level of central regulation of water–electrolyte homeostasis, for a transient disturbance of the steroid hormone balance in the early postnatal period leads to changes in function of the hypothalamic centers controlling several other functions [4, 6].

The aim of the present investigation was to study the age dynamics of the content of neurosecretion in the posterior lobe of the pituitary in intact rats and to determine the ADH content in the neurohypophysis of adult rats, induced by hydrocortisone at different times of postnatal ontogeny.

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