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CHOLINERGIC AND GABA-ERGIC MECHANISMS CONTROLLING MENTAL RESPONSES IN RATS IN THE EARLY POSTNATAL PERIOD

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KEY WORDS: motor reactions; early postratal growth; GABA-ergic drugs; cholinomimetics; cholinolytics.

In the early postnatal period rats show significantly more motor responses (MR) of the twitch type during sleep than adult animals. Previous investigations showed correlation between the onset of MR of the twitch type and periodic formation of a state of hypoxemia [5].

It is interesting to study the pattern of neurohumoral regulation of MR of the twitch type in rats in the early postnatal period. Significantly higher acetylcholinesterase activity is found in the blood and various parts of the brain of animals at an early age than in adults [6], and this is associated with a low level of inhibitory cholinergic processes in the CNS [1, 2, 8], and also evidently of GABA-ergic mechanisms.

The object of this investigation was to study the role of the above-mentioned mediator systems as factors involved in the neurohumoral regulation of MR of twitch type in rats in the early postnatal period.

EXPERIMENTAL METHOD

The frequency of MR of twitch type was analyzed in noninbred albino rats from the 1st through the 30th day of life. In addition the action of drugs on the character of performance of MR of twitch type was investigated in rats aged 12 days. The MR were recorded by means of special transparent plastic cages to the floor of which piezoelectric transducers were fixed on the outer side. MR (actogram) were evaluated on the ÉÉGP4-02 electroencephalograph. The cages were heated by means of an electric lamp to 25°C. At this temperature the rats quickly fell asleep and began to exhibit MR of twitch type. To analyze the mechanisms of regulation of MR, rats in the experiments of series I were given an intraperitoneal injection of the GABA preparation aminalone (50 mg/kg) and the GABA derivative fenibut (5 mg/kg) [7], and also diazepam (0.3 mg/kg). The last of these drugs increases the sensitivity of receptors to GABA but in large doses it delays GABA deactivation [3] and potentiates GABA-ergic inhibition [3, 9]. In the experiments of series II drugs increasing the acetylcholine concentration were injected into the rats: neostigmine (0.6 mg/kg) and galanthamine (0.1 mg/kg). In series III the action of the muscarinic cholinolytic atropine (0.02 mg/kg) was analyzed. These drugs were dissolved in physiological saline and injected intraperitoneally in a volume of 0.1-0.2 ml. The order of the investigation was as follows. First the initial frequency of MR was recorded, this was repeated after injection of physiological saline, and again af-

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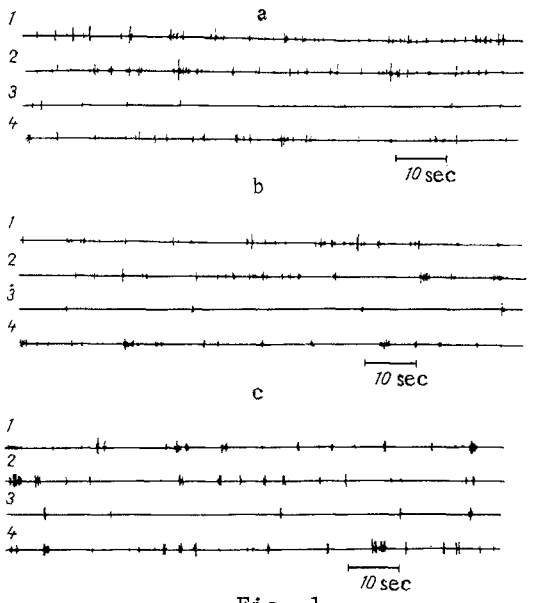

Fig. 1

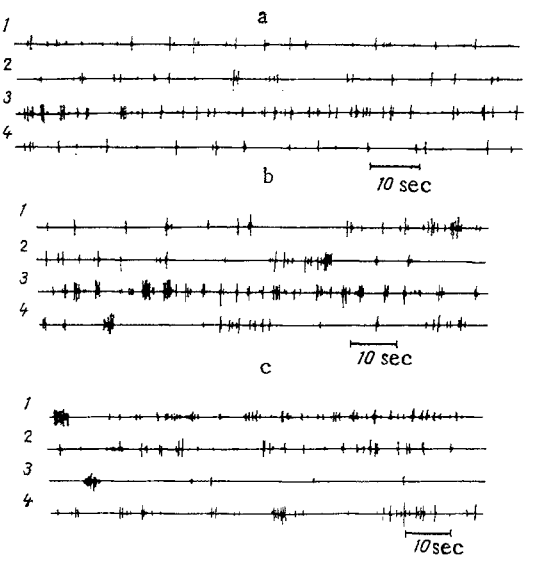

Fig. 2

Fig. 1. Actogram of MR of twitch type in rats aged 12 days after injection of aminalone (a), fenibut (b), and diazepam (c). 1) Initial actogram; 2) after injection of physiological saline; 3) after injection of drug; 4) 30 min after injection of drug.

Fig. 2. Actogram of MR of twitch type in rats aged 12 days after injection of neostigmine (a), galanthamine (b), and atropine (c). 1) Initial actogram; 2) after injection of physiological saline; 3) after injection of drug; 4) 30 min after injection of drug.

ter injection of the drug, and finally MR again were recorded 30 min after injection of the drug. The total number of rats used in the experiments was 56.

EXPERIMENTAL RESULTS

Starting from the 9th day of life the rats showed a significant ($P < 0.001$) decrease in the frequency of MR of twitch type from 832 ± 59 (9 days old) to 623 ± 3.8/h (12 days old). During growth and development the frequency of MR continued to fall to 76 ± 8/h at the age of 30 days ($P < 0.001$).

Aminalone reduced the frequency of MR of twitch type in rats aged 12 days from 624 ± 4.1 to 596 ± 6.3/h ($P < 0.001$, Fig. 1a). After injection of fenibut the frequency of MR also fell from 623 ± 4.1 to 384 ± 6.1/h ($P < 0.001$, Fig. 1b). Injection of diazepam into 12-day-old rats had the same effect on the frequency of MR of twitch type as aminalone and fenibut, reducing it from 631 ± 5.1 to 602 ± 4.8 MR/h ($P < 0.001$, Fig. 1c). These data are evidence that the decrease in frequency of MR of twitch type during postnatal ontogeny is evidently connected with potentiation of the mechanisms of inhibition in the CNS and, in particular, with an increase in GABA synthesis.

The cholinomimetic neostigmine caused an increase in the frequency of MR of twitch type from 625 ± 4 to 683 ± 5.1/h ($P < 0.001$, Fig. 2a). After injection of galanthamine the frequency of MR increased from 618 ± 5.3 to 676 ± 3.8 MR/h ($P < 0.001$, Fig. 2b). The muscarinic cholinolytic atropine reduced the frequency of MR of twitch type in rats 12 days old from 623 ± 1.08 to 582 ± 4.2/h ($P < 0.001$, Fig. 2c).

Injection of drugs increasing the acetylcholine concentration thus causes an increase in the frequency of MR of twitch type in rats in the early postnatal period. Conversely, injection of the muscarinic cholinolytic led to a decrease in the frequency of MR. Consequently, the high frequency of MR of twitch type in the early postnatal period is the result of the particular relationship between cholinergic and GABA-ergic mechanisms of regulation during this period, with functional predominance of the cholinergic system.

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ELECTROPHYSIOLOGICAL ANALYSIS OF ADRENERGIC MECHANISMS OF HYPOTHALAMIC CONTROL OF THE MALE GONADS

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KEY WORDS: hypothalamus; arcuate region; unit activity; testosterone propionate; rausedil.

One method of identifying the transmitter nature and determining the role of various neuronal components of hypothalamic structures responding to testosterone in the mechanism of tonic control and regulation of the male gonads on the negative feedback principle is to study spontaneous spike discharges (SD) of neurons of these structures during artificial hyperandrogenization, against a background of selective weakening of mediator systems. The most interesting region from this point of view is the arcuate region (AR) of the median eminence of the hypothalamus. On the one hand, its role in the production of gonadotrophin-releasing factors and its predominantly dopamine mechanisms of mediation are well known [1, 3]; on the other hand, the quite extensive polyfunctional afferent-efferent connections of AR neurons and their hormonal polyvalency suggest that its function is the result of complex interaction between its polyfunctional components.

The aim of this investigation was to study changes in spontaneous SD of AR neurons in the hypothalamus in response to testosterone, injected against the background of pharmacologic inhibition of adrenergic mechanisms by rausedil, which exhausts presynaptic catecholamine depots [2, 6].

EXPERIMENTAL METHOD

Experiments were carried out on sexually mature male rats immobilized with tubocurarine. SD of AR neurons in the hypothalamus were recorded extracellularly by means of stereotaxically implanted [7] glass microelectrodes (diameter of tip 4-5 μ), filled with 3 M NaCl (resistance not more than 1 MΩ). SD were photographed from the screen of an S1-18 oscilloscope by means of an FOR-2 camera. Hyperandrogenization was carried out by intramuscular injection of an oily solution of testosterone proprionate in a dose of 30 mg/kg body weight. SD were recorded for 3 h after injection of the compound. For each experiment separately and for all experiments of each series together the mean discharge frequency was calculated before and after administration of testosterone. The significance of differences was calculated by Student's t test [5].

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