LITERATURE CITED

1. T. A. Adzhimolaev, "Electrophysiological characteristics of the formation and transformation of activity of the neuromuscular system during postnatal ontogeny in mammals," Author's Abstract of Candidate's Dissertation, Moscow (1963).
2. E. V. Maksimova, Zh. Évol. Biokhim. Fiziol., 7, 162 (1971).
3. R. U. Ostrovskaya, G. M. Molodavkin, R. Porfir'eva, et al., Byull. Éksp. Biol. Med., No. 3, 50 (1975).
4. V. P. Praznikov, Fiziol. Cheloveka, No. 4, 668 (1981).
5. V. D. Rozanova, Outlines of Experimental Age Pharmacology [in Russian], Leningrad (1968).
6. B. A. Tolpyshev, Farmakol. Toksikol., No. 2, 140 (1980).
7. N. M. Yakovlev, Adaptive Mechanisms of Movement Control in Ontogeny [in Russian], Leningrad (1981).
8. E. Costa and P. Greengard, Adv. Biochem. Psychopharmacol., 14, 176 (1975).

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

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UDC 612.826.4-064:612.616.31].014.421.7-08

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].

Department of Pathological Physiology, Rostov Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR P. D. Gorizontov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 95, No. 3, pp. 18-19, March, 1983. Original article submitted June 28, 1982.

0007-4888/83/9503-0273$07.50

TABLE 1. Changes in Discharge Frequency of AR Neurons in Hypothalamus at Different Times after Injection of Testosterone Propionate (Series I) or of Peach Oil (Series III) Preceded by Administration of Rausedil

Series of experiments	Number of spikes per second				
	background	30 min	1 h	2 h	3 h
I	2,2±0,12 (119)	2,7±0,15 (110)	3,9±0,22 (102)	4,1±0,12 (93)	3,5±0,21 (98)
P	>0,05	<0,05	<0,01	<0,001	<0,01
III	2,5±0,15 (43)	2,2±0,22 (45)	2,6±0,23 (45)	2,3±0,13 (29)	2,3±0,37 (32)

Legend. Number of neurons in parentheses.

In the experiments of the main series (series I, 14 rats) the animals were given intramuscular injections of a solution of rausedil in a dose of 1 mg/kg daily for four days. After SD of all neurons observed during insertion of the electrode through AR had been recorded, the rats were given testosterone. Next, after 30 min and 1, 2, and 3 h repeated microelectrode excursions were made through AR and all neurons found were recorded. In three rats of this series, after a group of neurons had been found in the initial state, the depth of insertion of the microelectrode was kept unchanged and SD of these neurons were recorded throughout the experiment.

The results of series I were compared with those of experiments in which SD were studied in intact animals (series II, 8 rats).

Control experiments (series III, 8 rats) were carried out on animals loaded with rausedil and receiving an intramuscular injection of 0.05 ml of peach oil. Activity of the same neurons was recorded in three of these rats throughout the experiment. At the end of each experiment the location of the microelectrode track in the AR zone was verified morphologically.

EXPERIMENTAL RESULTS

Administration of rausedil created a unique type of spontaneous firing pattern, characterized by a threefold reduction in the discharge frequency of AR neurons compared with that in intact animals (2.2 ± 0.12 and 7.0 ± 1.0 spikes/sec, respectively), with at the same time a decrease in the number of discharging neurons. For instance, in the course of one excursion through AR by the microelectrode activity was recorded in 3-4 times fewer neurons than in the intact animal. Injection of testosterone against this background, starting from the 30th minute, led to an increase in discharge frequency compared with the initial state (Table 1).

Similar changes in the mean discharge frequency also were found in cases when SD were recorded throughout the experiment from the same neurons. This trend of the changes in spike generation is diametrically opposite to the response of AR neurons of the intact brain to testosterone [1]. The action of testosterone on AR neurons, when preceded by exhaustion of presynaptic catecholamine (especially dopamine) depots is thus directly opposite to the effect of testosterone on the intact hypothalamus.

These results are evidence that the direct or indirect effect of testosterone on AR leads to inhibition of spontaneous SD of those catecholaminergic neurons which evidently constitute one of the mechanisms of negative feedback in the male hypothalamic-hypophyseal-gonadal system.

The results also suggest that in AR there is a certain number of neurons (possibly of different mediator nature) whose spontaneous discharge is not inhibited by rausedil, and which have the ability to potentiate SD in response to testosterone. An indirect argument against this hypothesis is the fact that no neurons with a discharge frequency of about 2 spikes/sec could be found in AR of intact animals.

The following suggestion may be put forward by way of explanation: Since the degree and rapidity of exhaustion of catecholamine depots in neurons may differ, neurons experiencing a smaller mediator deficit may preserve their ability to discharge, but on a more economical schedule. These low-activity neurons, according to the rule of the initial state, may respond by increased SD to adequate stimuli.

Realization of negative feedback from hypothalamic AR is evidently based on an integrative mechanism of interaction between neurons that are evidently by no means equivalent either

functionally or, perhaps, from the mediator point of view, and the resultant effect of the hypothalamus on the gonads may be modulated to some extent not only by adrogens, but also by other factors.

The authors are grateful to Professor A. B. Kogan, Director of the Research Institute of Neurocybernetics, Rostov University, and to Senior Scientific Assistant A. G. Sukhov for help with this investigation.

LITERATURE CITED

1. V. N. Babichev, The Neuroendocrinology of Sex [in Russian], Moscow (1981).
2. N. V. Vysotskaya, É. Sh. Matlina, V. V. Men'shikov, et al., in: Biogenic Amines [in Russian], Moscow (1967), p. 162.
3. P. A. Vunder, Self-Regulation Processes in the Endocrine System [in Russian], Moscow (1965).
4. The Pituitary-Adrenal System and the Brain [in Russian], Leningrad (1976).
5. G. F. Lakin, Biometrics [in Russian], Moscow (1980).
6. V. G. Shalyapina, Probl. Éndokrinol., No. 2, 60 (1970).
7. E. Fifkova and J. Maršala, Stereotaxic Atlas of Subcortical Structures of the Rat, Rabbit, and Cat Brain, Prague (1960).