ELECTROPHYSIOLOGICAL ANALYSIS OF THE STATE OF THE AUTONOMIC NERVES IN EXPERIMENTAL THYROTOXICOSIS

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UDC 616.441-008.61-092.9-07 : 616.839-073.9

Experimental thyrotoxicosis in rabbits is accompanied by increased excitability and decreased amplitude of potentials in the vagus nerve, the superior cervical sympathetic ganglion, and the postganglionic sympathetic trunk. The lability and functional stability of the sympathetic ganglion are reduced.

Previous experiments [7] have shown that experimental thyrotoxicosis in rabbits is accompanied by a decrease in spontaneous activity of the vagus nerve and of the postganglionic trunk of the superior cervical sympathetic ganglion (SCSG).

The object of this investigation was to study some parameters characterizing the functional state of the autonomic nerves.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 3.5-4 kg. Thyrotoxicosis was produced by administration of increasing doses of thyroid extract for 2 and 4 weeks [3]. The method of isolation of the nerves was described previously [7]. The threshold of stimulation, the latent period, the amplitude and duration of the action potentials, and the relative and absolute refractory periods in the vagus nerves, the SCSG, and its postganglionic trunk were investigated by supramaximal stimulation of the corresponding structures with square pulses (0.1 msec, 0.3/sec). To measure the lability of the SCSG, series of pulses ranging from 10 to 200/sec in frequency were applied for 10 sec to the preganglionic trunk. The measure of lability was the frequency of stimulation at which individual response potentials disappeared. Functional stability was characterized by the time from the beginning of stimulation (30/sec) to the development of a "pessimal" response (a decrease in amplitude of the response potentials by $\frac{1}{3}$ of its initial value) [1, 5]. Postactivation potentiation in the ganglion was investigated by stimulation of the preganglionic trunk (500 Hz, 50 sec) followed by application (5 sec later) of a test pulse. Recordings were made with a Disa-Electronic universal two-channel oscillograph with UBP1-02 preamplifier.

EXPERIMENTAL RESULTS

The results of investigation of the state of the vagus nerve are given in Table 1. Thyrotoxicosis in rabbits was accompanied by a decrease in the threshold and amplitude of the action potential. Its duration also was reduced, evidently because of shortening of the relative refractory period of the nerve. Although its value in the experimental animals was less than in the controls, the difference was not statistically significant.

The results of analysis of the state of the SCSG are given in Table 2. During progression of the thyrotoxicosis the excitability of the ganglion increased (threshold was lowered) and the duration of the

Laboratory of Pathophysiology, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Yudaev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 69, No. 5, pp. 35-38, May, 1970. Original article submitted October 10, 1969.

TABLE 1. Indices of Functional State of the Left Vagus Nerve in Rabbits

Index tested	Control (n = 9), M±m	Thyrotoxicosis				
		2 weeks (n = 9)		4 weeks (n = 9)		
		M±m	P	M±m	P	P_1
Latent period (in msec)	1.24±0.02	1.27±0.05	0.6	1.21±0.14	0.9	0.9
Amplitude of response potential (in mV)	1.84±0.2	1.47±0.07	0.09	1.04±0.02	< 0.001	< 0.001
Threshold (in V)	0.64±0.06	0.50±0.06	0.1	0.35±0.03	0.001	< 0.05
Duration of response potential (in msec)	2.98±0.15	2.93±0.14	0.8	2.52±0.15	< 0.05	0.06
Relative refractory period (in msec)	4.61±0.2	4.14±0.3	0.2	3.10±0.2	< 0.001	< 0.01
Absolute refractory period (in msec)	1.52±0.03	1.46±0.04	0.2	1.47±0.02	0.1	0.9

Note. Here and in Tables 2 and 3, P is the criterion of significance of differences between the control and experimental groups, and P_1 is the same between two experimental groups.

TABLE 2. Indices of Functional State of SCSG in Rabbits (potentials recorded from postganglionic trunk during stimulation of preganglionic trunk)

Index tested		Control M±m	Thyrotoxicosis				
			2 weeks		4 weeks		
			M±m	P	M±m	P	P_1
Latent period (in msec)		4.35±0.05	4.29±0.03	0.3	4.29±0.03	0.3	1
Amplitude of response potential (in mV)		185.5±9	162.7±13	0.15	132.8±9.2	< 0.001	0.09
Threshold (in V)		0.53±0.08	0.47±0.03	0.5	0.31±0.03	< 0.001	< 0.001
Duration of response potential (in msec)		2.83±0.1	2.71±0.1	0.4	2.60±0.1	0.1	0.4
Relative refractory period (in msec)		17.6±0.5	16.3±0.9	0.2	14.9±0.7	0.007	0.2
Absolute refractory period (in msec)		4.8±0.25	4.6±0.3	0.5	4.1±0.15	< 0.05	0.1
Functional stability (in sec)		14.7±0.3	12.2±1		9.3±1.3	0.001	0.09
Lability (pulses/sec)		37.4±2.3	44.6±3.3	0.09	33.5±3.3	0.3	< 0.001
Postactivation potentiation	%	397±40	305±27	0.08	187±3	< 0.001	0.002
	frequency of cases	6 of 15	7 of 9	0.15	9 of 9	< 0.01	

refractory period was reduced. The latter suggests shortening of the duration of the action potential itself in the ganglion cells. However, because of the experimental conditions, this index could not be assessed in the postganglionic fiber only. The decrease in amplitude of the recorded potential, clearly visible in the later stage of the pathological condition, could have been due either to a decrease in the number of cells responding synchronously to stimulation of the preganglionic trunk, or to a decrease in amplitude of the potentials generated by each single cell. Finally, it could have been the result of ionic changes on the membranes of fibers of the postganglionic trunk cells. To investigate this problem, the phenomenon of postactivation potentiation was studied. As the severity of the thyrotoxicosis increased, this phenomenon became more easily reproducible. On the assumption that postactivation potentiation is based on synchronization of the response of cells to the test stimulus, the results obtained must indicate the existence of conditions in thyrotoxicosis facilitating such synchronization. However, the degree of postactivation potentiation was lower in the experimental animals than in the controls (in cases in which it could be repro-

TABLE 3. Indices of Functional State of Postganglionic Trunk of SCSG in Rabbits

Index tested	Control (n = 9), M±m	Thyrotoxicosis				
		2 weeks (n = 9)		4 weeks (n = 9)		
		M±m	P	M±m	P	P_1
Latent period (in msec)	1.3±0.03	1.2±0.01	0.7	1.3±0.03	1	0.9
Amplitude of response potential (in mV)	1.68±0.07	1.58±0.13	0.5	1.32±0.07	0.002	0.1
Threshold (in V)	0.69±0.1	0.45±0.07	0.06	0.36±0.03	0.005	0.2
Duration of response potential (in msec)	2.83±0.1	2.71±0.1	0.4	2.60±0.1	0.1	0.4
Relative refractory period (in msec)	4.6±0.25	3.9±0.25	0.18	3.2±0.29	0.002	0.4
Absolute refractory period (in msec)	1.38±0.17	1.29±0.17	0.7	1.29±0.17	0.7	1

duced). These results suggest that the decrease in amplitude of the action potential was due, not to a decrease in the number of ganglion cells responding during thyrotoxicosis to preganglionic stimulation, but rather to a decrease in voltage of the potentials generated by each single cell of the ganglion.

Experimental thyrotoxicosis was accompanied by phasic changes in lability of the SCSG; in the later stage this index was significantly lower than in the earlier stage of the pathological condition. The contradiction between the decrease in lability of the ganglion and the shortening of its refractory period is evidently attributable to differences in the methods used to determine each of these parameters. Investigation of lability 10 sec after the beginning of serial stimulation evidently led to the development of fatigue of the ganglion cells. Further evidence of the more rapid onset of fatigue in the SCSG in thyrotoxicosis was given by the results of determination of its functional stability: in the experimental animals the time taken for development of the "pessimal" response of the ganglion cells was reduced.

These results on the whole agree with those of Babichev's experiments [1], in which the state of the sympathetic ganglia in cats was studied during brief administration of thyroxine.

Results of assessment of the functional state of the postganglionic trunks of SCSG are given in Table 3. On the whole they correspond to the results obtained for other autonomic structures.

Experimental thyrotoxicosis in rabbits is thus accompanied by marked disturbances of conduction in autonomic nerves. These disturbances are characteristic of a decrease in the membrane potentials of the investigated structures, in agreement with results obtained in the writers' laboratory on excitable cells of a different model, myocardial cells [2]. Disturbances of this type are evidently based on changes in transmembrane ion gradients [4], due to the inadequate supply of energy for work of the potassium-sodium pump in thyrotoxicosis [6].

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