A Study of the Vagus Tone

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According to current notions, the centers of the vagus nerves, which decelerate the work of the heart, are constantly in a state of tonic excitation; therefore, the heart rate (HR) increases for a decrease of their tone and drops for an increase of their tone [1-3, 7]. The main evidence of the presence of vagus tone is the development of tachycardia after transection of the nerves or their switching off by atropine [1, 2, 7, 12]. At the same time, pharmacologic blocking of the sympathetic nerves does not arrest or prevent the above-mentioned tachycardia [2].

However, in the opinion of other researchers [6, 8, 9], vagotomic and atropine tachycardia result from stimulation of the sympathetic nervous system, and not from the switch-off of the inhibitory vagus tone, since not only efferent, but also afferent fibers are switched off after vagotomy. Several times as many of the latter are contained in the vagus [10]. Atropine, moreover, stimulates the sympathetic nervous system by acting directly on the central nervous system (CNS) [8, 9]. The arrest or prevention of vagotomic tachycardia in experimental animals by surgical desympathization corroborates such a conclusion [8, 9, 11].

Thus, it is unclear why pharmacologic desympathization does not arrest vagotomic tachycardia, whereas surgical intervention does. The aim of our study was to investigate the causes of the above contradiction and to elucidate the role of the sympathetic and parasympathetic nerves in the regulation of cardiac activity.

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MATERIALS AND METHODS

The experiments were carried out on albino laboratory rats, wild pigeons, rabbits, and guinea pigs under conditions of the surgical stage of urethane (2 g/kg), hexenal (50-70 mg/kg), or nembutal (40-50 mg/kg) anesthesia for intraperitoneal (rats, rabbits, and guinea pigs) or intramuscular (pigeons) administration of the preparations. In the experiments on pigeons only urethane was used. One series of experiments was carried out on hens without anesthesia and without any surgical intervention. The electrocardiogram (ECG) and arterial pressure in the common carotid artery were recorded with the aid of an EMT-35 electronic transducer, a UBP2-03 amplifier of biopotentials, and an H327-5 ink recorder. In rats the sympathetic nervous system was switched off by ornidine (25 mg/kg, intraperitoneally). The vagus nerves were exposed and transected in the neck zone. An AID-3 apparatus was used for artificial ventilation. The HR was repeatedly calculated at the beginning of the surgical stage of anesthesia (in order to reveal any background instability), as well as after transection of both vaguses, and 25-40 min after ornidine injection. The indexes obtained 10 min after vagotomy were analyzed. All the results were statistically processed using Student's t test.

RESULTS

Since pharmacologic switch-off of the sympathetic nervous system did not arrest vagotomic tachycardia [2], while surgical intervention did [8,9,11], we suggested that the cause of the tachycardia arrest in the latter case is not the switching off of the

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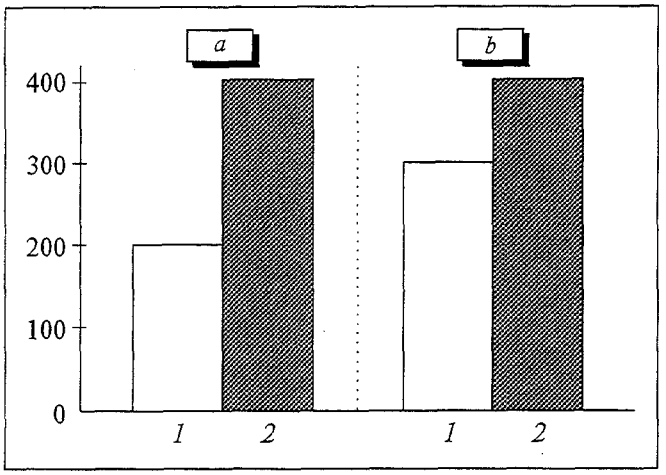

Fig. 1. Variation of HR (beats/min) in pigeons under different conditions. *a*: *1*) background HR; *2*) after ALV was switched on and both vaguses were transected (strong acceleration). *b*) *1*) against the background of ALV: markedly pronounced tachycardia; *2*) after transection of vaguses, ALV being continued (slight additional acceleration of heartbeats).

sympathetic nervous system, but surgical intervention per se.

This hypothesis was verified in experiments in which pharmacologic and surgical switch-off of the sympathetic and parasympathetic nervous system was performed. Even such a mild surgical intervention as that of exposing the vaguses in the neck zone and recording the arterial pressure in the common carotid artery reduced the vagal tone, which was manifested as an increased HR in the animals. In particular, in rats under urethane (8 animals), nembutal (9), or hexenal (8) anesthesia the HR increased by 16% on the average (from 312±9 to 362±16 beats/min).

According to our findings, an even more marked reduction of the tone was caused by the exposure in experiments on pigeons. In several series of experiments we discovered that during the surgical stage of urethane anesthesia the HR was 163±11 beats/min (the statistical mean HR). It was liable to be higher or lower in different groups of animals. Specifically, in one series of experiments the background HR in pigeons was 138±4 beats/min, and the exposure of both vaguses in the neck zone raised this parameter to 205±18 beats/min, i.e., by 48% ($p<0.001$). In another series of experiments, just a slight complication of the operation (exposure of the right carotid artery and recording the arterial pressure in it being added to exposure of the vaguses) raised the HR more markedly in 11 pigeons (to 248±23 beats/min), and the subsequent transection of both vaguses in these animals was attended by an increase in the HR to 362±20 beats/min (61%, $p<0.001$). Switching off the vaguses with the use of atropine (only the ECG was recorded) raised the HR in 35 pigeons 2-fold: from 159±11 to 328±14 beats/min (by 113%, $p<0.001$). The data obtained provide evidence that tachycardia caused by surgical interventions, as well as the additional heartbeat acceleration following vagotomy, may be the result of either a reduction of vagus tone or stimulation of the sympathetic nervous system.

However the sympathetic origin of vagotomic and atropine tachycardia [6,8,9] is ruled out by the results of our experiments, in which we established that tachycardia also developed in the experimental animals under conditions of pharmacologic blocking of the sympathetic nervous system. For instance, in 10 rats against the background of ornidine (25 mg/kg), which reliably switched off the sympathetic nervous system, the HR was 336±15 and, after atropine injection, it increased to 436±13 beats/min (by 30%, $p<0.001$), while in 6 other rats the HR was 317±19 beats/min against the background of ornidine and increased to 424±6 beats/min (34%, $p<0.001$) after transection of both vaguses. According to these results the vagus tone is not markedly pronounced in rats, and therefore surgical and mild pharmacologic inhibition of the vaguses caused approximately similar tachycardia.

The data obtained indicate that both vagotomic and atropine tachycardia result from the switch-off of the inhibitory tone of the vaguses, and not from the stimulation of the sympathetic nervous system, as was suggested by a number of scientists [6,8,9].

TABLE 1. Individual Differences of Responses to the Switch–Off of the Vagus Nerves in Pigeons

№ of experiment	Sex	Weight, g	Anesthesia (i.m.), g/kg	Mode of vagus switch-off	Background HR, beats/min	Result	
						HR, beats/min	%
125	M	325	Urethane, 1	Indomethacin, 2 mg/kg, i.m.	129	159	23
155	M	350			129	354	174
156	M	350			135	465	244
187	F	230	Urethane, 2	Atropine, 2 mg/kg, i.m.	138	201	45
158	F	225			135	384	184
26	M	270	Urethane, 2	Vagotomy	204	225	25
110	M	380			225	462	102

Arrest of vagotomic tachycardia by desympathization of animals in the experiments performed by these scientists is, according to our findings, a result of surgical interventions.

It must also be taken into account that the tachycardia resulting from the exposure or switching off of the vagus nerves starts to diminish after 10 min, and the HR may revert to the initial level.

In acute experiments artificial lung ventilation (ALV) is often used after the exposure, and we speculated that this, too, can affect the strength of the vagus tone. This assumption was verified in the next series of experiments by switching on ALV before or after the transection of the vaguses. After both vagus nerves were exposed and the recording of the blood pressure was instituted in the common carotid artery, the HR constituted 202±17 beats/min; after ALV was switched on, it increased to 311±28 beats/min (54%) and, after bilateral vagotomy, to 386±17 beats/min (i.e., by only 24%) (Fig. 1). In these experiments ALV per se caused a severe tachycardia due to a decrease of the vagus tone, and therefore transection of the vaguses just resulted in an insignificant (24%) increase of the HR (in pigeons the HR increased by 113% for switching off the vagus nerves by atropine without any surgical intervention and without ALV).

If, however, ALV was switched on after the vagus nerves were transected, the differences between the experimental results were markedly pronounced. In the next series of experiments, after the exposure of the vagus nerves, the HR in 14 pigeons was 198±9 beats/min, while after their transection and subsequent switching on of ALV, it rose to 383±11 beats/min (i.e., increased by 94%, $p<0.001$), this being four times as high as for vagotomy under conditions of preliminary ALV (24%). The maximal HR after switching on ALV and after vagotomy was approximately the same in both cases: 370-390 beats/min, irrespective of whether vagotomy or ALV was performed first (Fig. 1).

Species-specific, sexual, and even individual differences proved to exist with respect to the strength of the vagus tone. For instance, in our experiments vagotomy raised the HR in 12 pigeons from 189±7 to 376±16 beats/min (by 99%, $p<0.001$); in 15 rats this increase was markedly smaller: from 346±13 to 447±13 beats/min (by 29%, $p<0.001$); in 12 guinea pigs the HR rose just 5%: from 315±17 to 331±22 beats/min ($p>0.5$); and in 13 rabbits this parameter was unchanged: 286±6-284±7 beats/min (Fig. 2).

The switch-off of the vagus nerves by atropine is known to cause tachycardia in cocks, but not in hens [4]. On the basis of this fact, we carried out 40 chronic experiments on 5 cocks and 5 hens (9 months old). The experiments were performed without anesthesia and without surgical interventions, that is, under conditions which rule out the effect of extreme factors and emotional excitation on the vagus tone. Each bird was involved in the experiment 4 times with a 3-4-day interval. In the first experiment all individuals were intramuscularly administered 0.5 mg/kg indomethacin, in the second 0.5 mg/kg atropine, in the third 2 mg/kg atropine, and in the fourth 2 mg/kg indomethacin; within the given limits, the differences in the doses of preparation did not affect the results of the experiments. During the experiment, the animal was in a calm state and natural position, with the legs bandaged and the wings fixed with a Pean clamp. Indomethacin was found to raise the HR in cocks 3 times as much (from 247±8 to 351±7 beats/min, by 42%, $p<0.001$) as in hens (from 310±11 to 351±12

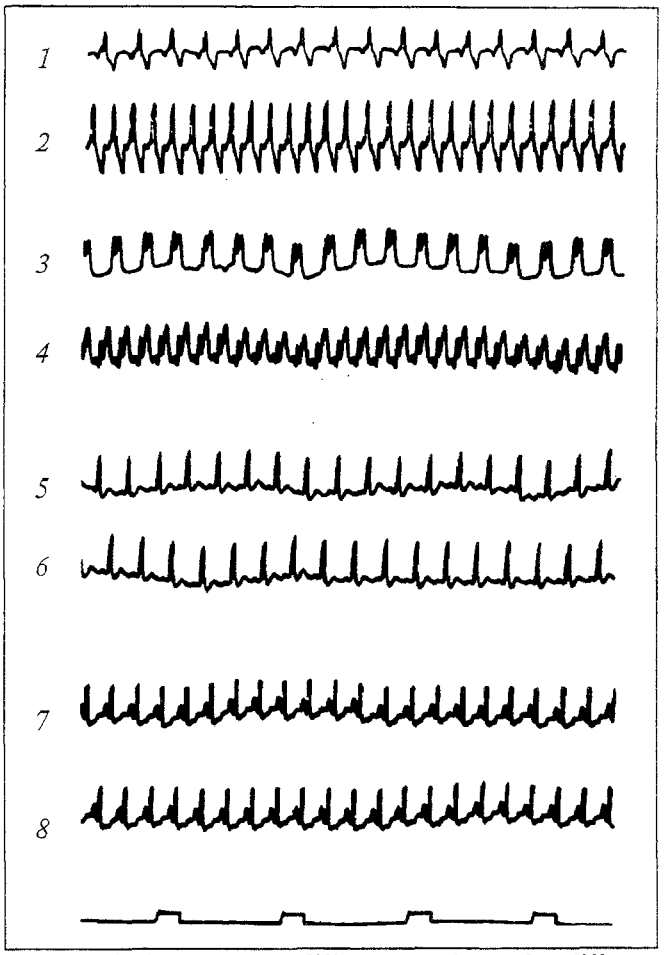

Fig. 2. HR in animals of different species under different conditions (ECG records). *1*, *3*, *5*, and *7*) before vagotomy; *2*, *4*, *6*, and *8*) after vagotomy. *1* and *2*) pigeon: strong acceleration; *3* and *4*) rat: slight acceleration; *5* and *6*) rabbit: unchanged; *7* and *8*) guinea pig: unchanged.

beats/min, by 13%, $p<0.01$), while atropine virtually did not change the HR in hens (307±7 vs. 324±13 beats/min), and caused a 3 times smaller increase in the HR than indomethacin did in cocks (249±8 vs. 288±18 beats/min, by 15%, $p<0.05$). The results obtained attest to a sexual difference in the strength of the vagal tone, which, naturally, must be taken into account. These data also rule out the suggestion [8,9] that atropine provokes tachycardia due to a direct action upon the CNS and by stimulating the sympathetic nervous system. Indomethacin is known not to exhibit such properties [5], but it causes even stronger tachycardia than atropine, this being evidence of the parasympathetic origin of the tachycardia arising following the switch-off of the vagus nerves.

Individual differences are also observed in the cardiac responses to the switch-off of the vaguses, as is shown in Table 1. All conditions in these pairs of experiments were the same, while their results were different, an outcome which was determined by diverse strength of the vagus tone in individual subjects.

Thus, the leading role in the development of vagotomic and atropine tachycardia is played by the arrest of the inhibitory tone of the vagus, and not by the excitation of the sympathetic nervous system. The current notions on the vagus tone and its role in the regulation of cardiac activity are valid. Judging by our findings, the contradictory opinions on the vagus tone result from underestimation of a number of factors relating to the experimental conditions.

REFERENCES

1. I. A. Arshavskii, in: *Self-Regulation of the Heart* [in Russian], Moscow (1967), pp. 13-15.
2. G. P. Konradi, in: *Circulation Physiology: Heart Physiology* [in Russian], Leningrad (1980), pp. 400-411.
3. G. I. Kositskii (Ed.), *Human Physiology* [in Russian], Moscow (1985).
4. L. M. Lepekhina, in: *Physiological Basis of Electrocardiography in Animals* [in Russian], Moscow-Leningrad (1965), pp. 72-79.
5. M. D. Mashkovskii, *Medicinal Preparations* [in Russian], Vol. 1, Moscow (1986).
6. M. G. Nikol'skaya, G. E. Samonina, and M. G. Udel'nov, *Fiziol. Zh. SSSR*, **60**, № 10, 1557-1562 (1974).
7. A. D. Nozdrachev (Ed.), *General Course of Human and Animal Physiology* [in Russian], Vol. 2, Moscow (1991).
8. M. G. Udel'nov, *Nervous Regulation of the Heart* [in Russian], Moscow (1961).
9. M. G. Udel'nov, *Physiology of the Heart* [in Russian], Moscow (1975).
10. E. Agostony, Y. E. Chinnock, and B. N. Daly, *Physiol.*, **135**, № 1, 182-205 (1957).
11. W. D. Bercowitz, B. S. Scherlag, T. E. Stein, and A. N. Dancato, *Circulat. Res.*, **24**, № 3, 447-455 (1969).
12. P. Duchene-Marrulas, J. *Physiol. (Paris)*, **66**, № 4, 373-397 (1973).