PHYSIOLOGY

The Study of the Sympathetic Nervous System Tone

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The majority of investigators consider that the sympathetic tone is weakly defined or is entirely absent, unlike the more pronounced vagus tone [1,2,5,7]. This is confirmed, in particular, by empirical data on the block of the sympathetic nervous system by reserpine or propranolol [6,8], which just slightly decreases the degree of the atropine- and vagotomy-induced tachycardia in dogs and cats.

Similar results were obtained in experiments with surgical cardiac desympathization: removal of both stellate ganglia, which project the sympathetic nerves to the heart, does not result in a stable bradycardia in experimental animals due to the absence or weak manifestation of the sympathetic tone [2].

However, there is an opposite view - namely, that the sympathetic nervous system tone is quite well pronounced. This conclusion is also supported by experimental findings [3,10,12]. An inhibition of the sympathetic nervous system activity causes in dogs a decrease of the heart rate from 100 to 60 beats/min, i.e., by 40%. This permanent effect of the sympathetic nerve is called sympathetic tone [3]. At rest the vagus nerve tone dominates that of the sympathetic, because the rhythm of the completely denervated heart (native rhythm) is substantially higher than that of the intact heart [3].Similar data on heart rate decrease by 25% after propranolol (β-adrenoblocker) injection were obtained by other investigators in dogs [11].

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The existence of a sympathetic tone is also attested by experiments performed under anesthesia at 20-25°C in crucian carp, which demonstrated a decrease of the heart rate by 22% after blockade of the β-adrenoreceptors by propranolol (1 mg/kg) [4]. The adrenergic innervation is revealed in all the heart chambers in these animals with the fluorescence technique [4]. According to some authors [9], the greatest sympathetic tone is observed in rabbits, rats, and hens.

Thus, the contradictory nature of the cited data motivated us to continue these studies in order to clarify the degree of sympathetic nerve tone and its significance for the regulation of heart activity.

MATERIALS AND METHODS

The experiments were carried out both on alert animals of different species (pigeons, rats, guinea pigs, and dogs) and under surgical anesthesia. Urethane was injected i.p. in a dose of 1.5-2 g/kg, pigeons were injected i.m., and dogs were treated with hexenal i.m. 70-100 mg/kg.

Chronic experiments on the alert animals were performed without anesthesia or any surgical manipulations. The animals were injected only drugs blocking either the sympathetic or the parasympathetic chain of the autonomic nervous system. In these experiments the animals maintained natural posture in a steady state: a dog was fixed in a stall with straps, a loosely bandaged pigeon was in a cotton "nest".

The registered indexes were as follows: electrocardiogram (ECG) and arterial blood pressure in the

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common carotid artery using an EMT-35 electronic sensor and H327-5 ink recorder. In each experimental series the control registration was performed repeatedly during 20-40 min until the minimal stable level of the heart rate was reached in the animals. The pharmacological agents were then injected.

The heart rate indexes were registered 10-15 min after inderal or methacin and 20-30 min after darenthin injection. The time was enough to achieve a blockade of the sympathetic and parasympathetic systems by the listed drugs.

RESULTS

In the first experimental series on 46 animals of different species (pigeons, rats, guinea pigs, and dogs), the optimal doses of pharmacological agents which reliably block the sympathetic and parasympathetic systems were determined. Only then it was possible to obtain convincing evidence of the degree of tone of one or another chain of the autonomic nervous system. The stellate ganglion or its heart branches were stimulated in situ before and after darenthin (5-30 mg/kg) or inderal (0.5-3 mg/kg) injection. The chosen drug dose did not result in a change of heart contraction under nerve stimulation. The vagus nerve was stimulated in the neck region.

It was established that darenthin reliably switches off the sympathetic system only in doses of 20-30 mg/kg, and inderal in doses of 1-3 mg/kg. The guinea pig sympathetic nerve is blocked reliably when inderal is injected i.v. in a dose of 1 mg/kg, and the same effect in pigeons is achieved by a dose of 2-3 mg/kg injected i.m.

The parasympathetic inhibitory effect related to vagus nerve stimulation is abolished by the M-cholinoblocker methacin injected i.m in a dose of 3 mg/kg in pigeons, and in dogs injected i.p. or s.c. (in the neck region). But the inhibitory effect of the natural impulse activity was completely blocked in pigeons (49 animals) by i.m. methacin injection in a dose of 2 mg/kg, which is confirmed by the stepped-up heart rate from 188±13 to 376±19 beats/min (100%, $p<0.001$) with an increase of the injected dose of methacin from 0.03 to 2 mg/kg. A further increase of the injected dose to 3 mg/kg does not elevate the heart rate (Fig. 1).

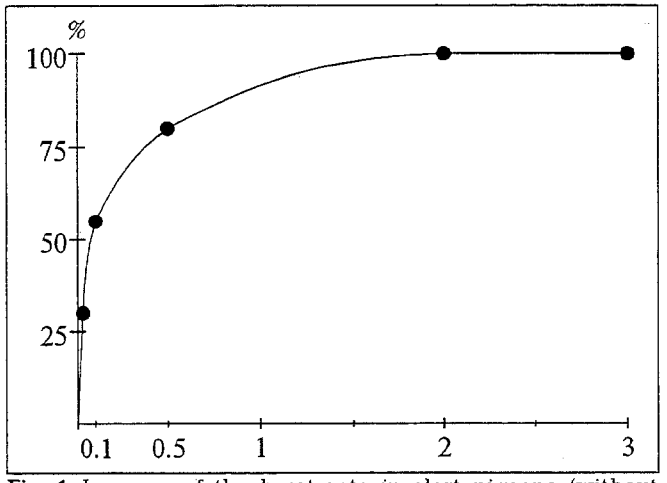

Fig. 1. Increase of the heart rate in alert pigeons (without anesthesia, at rest) as a result of an increase of indomethacin dose (i.m.) from 0.03 to 3 mg/kg (each point on the curve represents 8–10 experiments).

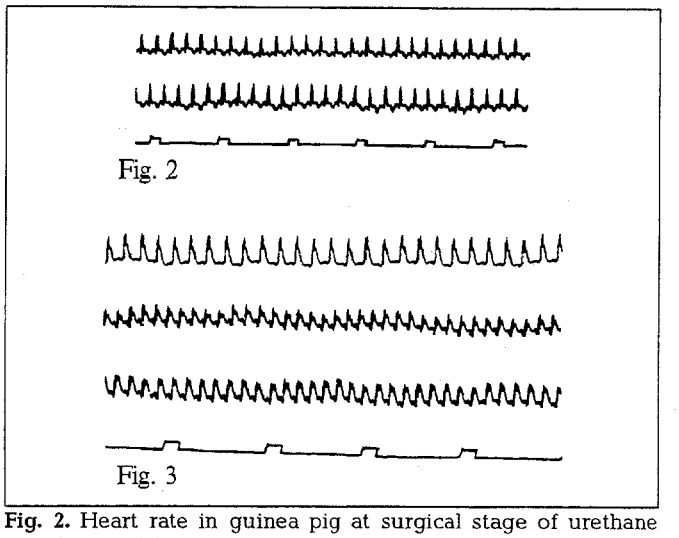

Fig. 2. Heart rate in guinea pig at surgical stage of urethane anesthesia. 1) before darenthin injection; 2) against darenthin background (without alterations). ECG recording. Time marker 1 sec.

Fig. 3. Heart rate in rat at surgical stage of urethane anesthesia. *1*) heart rate after dissection of both vagus nerves in neck region; *2*) tachycardia after cutting of both vagus nerves; *3*) after darenthin injection, without changes. ECG recording. Time marker 1 sec.

The sympathetic system tone was examined immediately after determination of the optimal drug doses.

The first experimental series was carried out on 16 albino rats and 10 guinea pigs under urethane anesthesia without any surgical manipulations. Darenthin-induced (i.p. 30 mg/kg) blockade of the sympathetic nervous system did not affect the heart rate (317±8 versus 315±7 beats/min) in guinea pigs (Fig. 2) and produced an unreliable increase of the heart rate in rats (327±17 versus 309±16 beats/min), the cause of which was not clear.

The problem was solved in 22 experiments with stimulation of the vagus nerve in rats, guinea pigs, and pigeons. It was established that darenthin strongly inhibited both vagus and sympathicus in pigeons. Darenthin did not affect the vagus-produced inhibition in rats and guinea pigs. However, under natural impulse activity darenthin can perhaps slightly reduce the inhibitory effect of the vagus nerve on heart activity in rats, which may manifest itself as just slight tachycardia.

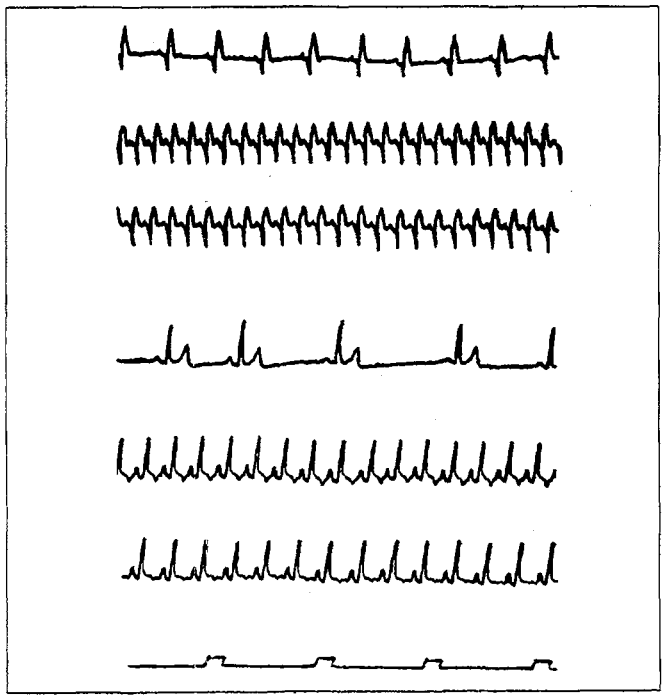

Fig. 4. Heart rate changes in alert pigeon (*1, 2, 3*) and dog (*4, 5, 6*) at rest without anesthesia. *1, 4*) background; *2, 5*) after methacin injection; *3*) after inderal injection (without changes); *6*) after darenthin injection (slight slowing). ECG recording. Time marker 1 sec.

In view of this, the next experimental series was performed on 8 rats after the preliminary cutting of both vagus nerves, so the heart rate under darenthin injection could change only due to the disengagement of the sympathetic nervous system. The experiments revealed that the vagotomy itself produced heart acceleration (469±11 versus 338±19 beats/min) (39% $p<0.001$), which points to an increased inhibitory vagus tonus in the rats. The subsequent abolition of the sympathetic effect with darenthin (30 mg/kg) resulted in a heart rate decrease only from 469±11 to 449±19 beats/min (5%, $p>0.01$), providing evidence that there is no sympathetic system tone in rats (Fig. 3).

Since it is well known that general anesthesia can markedly change the tonus of the brain and, naturally, of the autonomic nervous system, in order to clarify the degree of the sympathetic tone we performed further investigations under chronic conditions without any surgical manipulations or anesthesia. The only index recorded was ECG.

It was revealed that inderal injections (2-3 mg/kg) resulted in a decrease of the heart rate from 143±8 to 134±10 beats/min in 11 pigeons (6%, $p>0.2$). Darenthin injected in 11 dogs decreased the heart rate from 95±4 to 90±5 beats/min (5%, $p>0.2$).

To obtain more reliable results the last experimental series was performed on 7 pigeons and 9 dogs under preliminary blockade of the parasympathetic nervous system with methacin. It was revealed that methacin injection itself stepped-up the heart rate both in pigeons from 147±9 to 389±33 beats/min (165%, $p<0.001$) and in dogs from 89±6 to 248±11 beats/min (179%, $p<0.001$).

Subsequent sympathetic nervous system blockade with inderal against a methacin background decreased the heart rate in pigeons only from 389±33 to 366±34 beats/min (6%, $p>0.2$). The same darenthin-induced blockade in dogs resulted in a drop of the heart rate from 248±11 to 236±14 beats/min (5%, $p>0.1$, Fig. 4). These findings confirm that the vagus nerve tone in pigeons and dogs is clearly pronounced, while the sympathetic system tone is virtually unexpressed.

In fact, a decrease of the heart rate related to the abolition of the sympathetic nervous system was not observed at all in dogs and pigeons. Special experiments, performed on 8 pigeons and 9 dogs, demonstrated that 15-20 min after atropine injection the heart rate drops by itself without blockade of the sympathetic nervous system (in pigeons by 17, and in dogs by 6 beats/min). The heart rate is more stable during the period 10-15 min after atropine injection.

A pronounced (by 20-40%) decrease of the heart rate was revealed in dogs and fish by other investigators [3,4,9] under these conditions. According to our findings, this decrease does not relate to the abolition of the sympathetic nervous system, but is a result of the experimental conditions and, in particular, of the effects of general anesthesia, surgical manipulations, and, probably, hypothermia.

Thus, the tone of the sympathetic nerve is not pronounced and the heart rate at rest is regulated by the vagus nerve and humoral substances.

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