The Sympathetic Nervous System Is Not Implicated in the Development of Vagotomy-Induced Tachycardia

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It is believed by a number of investigators that vagal tone is weak and that tachycardia after bilateral vagotomy results from excitation of the sympathetic nervous system. However, this study shows that postvagotomy tachycardia develops without the participation of the sympathetic nervous system and decreases in the course of time spontaneously in animals with uninterrupted sympathetic nervous pathways. The degree of vagal tone is influenced by the type and depth of anesthesia.

Key Words: *heart; nervous regulation*

It is widely believed that the vagus nerve has a very pronounced inhibitory tone, as is evidenced, in particular, by the sharp rise in heart rate observed in animals after bilateral vagotomy [3,6,9]. Rendering the sympathetic nervous system (SNS) nonfunctional surgically or by drugs cannot prevent or abolish postvagotomy tachycardia [3]. This led investigators to conclude that nerve impulses which act to lower the heart rate and reduce vagal tone are being continuously conveyed via the vagus under natural conditions. The decrease in vagal tone results in a rapid rise of the heart rate, which is a phenomenon of extraordinary adaptive significance under diverse circumstances. According to most researchers, the parasympathetic tone predominates at rest in health, and this situation can only change as a result of interventions or disease [10].

However, other investigators [1,2,4,5] maintain that the vagal tone is weak and that the cause of tachycardia following vagotomy is SNS excitation developing because the heart is deafferented in the test animal. One of the arguments adduced to support this view is that vagotomy interrupts not only efferent but also afferent fibers within the vagus, whose number is thought by some [7] to exceed 14- to 15-fold that of efferent fibers. Indeed, as found in some experiments with awake rabbits [11] and awake dogs [12], simultaneous deafferentation of the aortal and carotid sinus reflexogenic zones increased the heart rate from 267 to 309 beats/min and from 81 to 137 beats/min, respectively. However, in a similar experiment performed on dogs by other investigators [8], the heart rate increased only from 89 to 105 beats/min.

It was also found [4,5] that surgical or pharmacological interruption of the sympathetic nerve supply to the heart prevents or abolishes postvagotomy tachycardia in dogs and cats.

It thus remains unclear why interruption of the sympathetic supply averted or eliminated postvagotomy tachycardia in some experiments [4,5] and failed to do so in others [3]. The aim of the experiments described here was to gain insight into the role of the vagus and sympathetic nerves in the regulation of cardiac activity.

MATERIALS AND METHODS

The experiments were carried out on rats, pigeons, and dogs in the surgical stage of general anesthesia produced by urethan (2 g/kg), Hexenal (50-80 mg/kg), or Nembutal (40-50 mg/kg). In addition,

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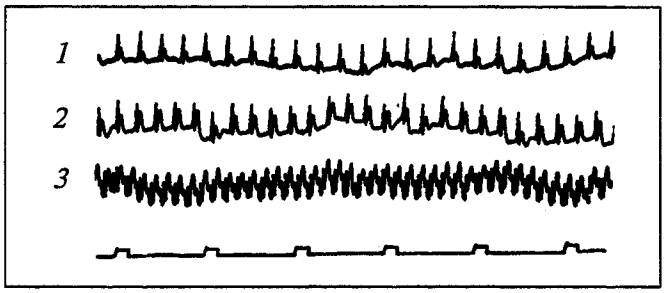

Fig. 1. Heart rate in a rat under urethan anethesia. *1*) before Ornid injection; *2*) after Ornid injection (no change); *3*) after bilateral vagotomy (increased rate). Shown here and in Fig. 2 are electrocardiographic tracings; time mark = 1 sec.

surface anesthesia with urethan (1 g/kg) was used in one series of tests on pigeons without any surgical interventions apart from drug injections. In all other tests, only a minimum of surgery was performed, namely dissection of the vagi followed by their transection before or after Ornid (bretylium tosylate) injection in a dose of 25 mg/kg that reliably blocks the SNS.

Changes in the heart rate were estimated from the ECG, which was recorded in the second standard lead in dogs and rats and in the cervicosacral lead in pigeons using needle electrodes inserted under the skin. In one series of tests, blood pressure was recorded in the common carotid artery. All drugs were injected intramuscularly in pigeons and intraperitoneally in rats and dogs. Heart beats were counted under anesthesia three times - after the cardiac rhythm had stabilized and a skin incision did not elicit a pain response (baseline heart rate) and then 20-30 min after Ornid injection and 10 min after vagotomy or atropine injection when the cardiac rhythm was already stable. The data were statistically analyzed using Student's *t* test.

RESULTS

Since surgical or pharmacological interruption of the sympathetic nervous pathways prevented or abolished postvagotomy tachycardia in some experiments [4,5] but not in others [3], we speculated that the result depends on the experimental procedures used (including the type of anesthesia) rather than on the interruption of the sympathetic supply. In the case of surgical interruption, the question arose as to whether it had been complete. To be on the safe side, we ensured in our own experiments a reliable and complete blockade of the SNS by pharmacological agents, bearing in mind, however, that the outcome of the experiment could be affected by other factors, such as dissection, the type and depth of anesthesia, and the time during which heart beats were counted after vagotomy. In this study we focused our attention on precisely these factors.

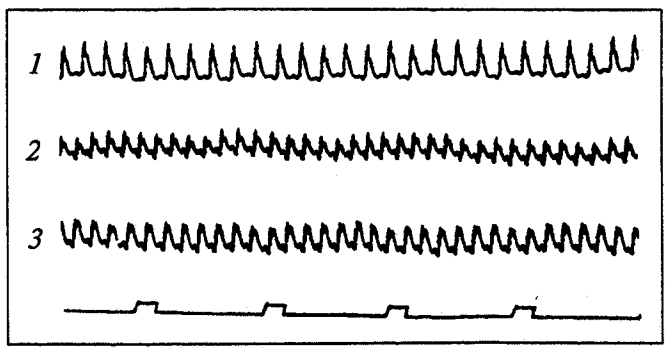

Fig. 2. Heart rate in a rat under urethan anesthesia. *1*) before vagotomy; *2*) after bilateral vagotomy (increased rate); *3*) after bilateral vagotomy and Ornid injection (no change).

In the first stage of the study, the relative contribution of the SNS to the development of postvagotomy tachycardia was determined in rats. In control tests using 6 rats, we found that postvagotomy tachycardia could also occur after preliminary blocking of the SNS with Ornid, i.e., exclusively because the inhibitory vagal tone was suppressed. Thus, the mean heart rate was 301±12 beats/min before Ornid injection and 317±19 beats/min postinjection, then rising to 424±19 beats/min (by 34%) after bilateral vagotomy ($p<0.001$) (Fig. 1). The contribution of the SNS to the development of postvagotomy tachycardia was determined in 8 rats with the sympathetic nerves blocked after bilateral vagotomy. In this experiment, the heart rate after the vagotomy increased from the baseline level of 338±19 to 469±11 beats/min, i.e., by 39% ($p<0.001$), and the subsequent Ornid injection lowered the heart rate by only 4% (from 469±11 to 449±19 beats/min; $p>0.1$) (Fig. 2). That the sympathetic nerve supply cutoff was complete was verified in separate tests: these did not show any increase in the frequency of heart beats when the stellate ganglion was stimulated in Ornid-injected rats.

Thus, as this experiment indicated, postvagotomy tachycardia arose because the inhibitory vagal tone was suppressed, whereas the contribution of the SNS to the tachycardia was extremely small. Subsequently we discovered that the tachycardia arising after the vagi were cut became progressively less severe even when the sympathetic nerve supply was not interrupted. In particular, we found in tests with 7 pigeons that the heart rate increased from the baseline level of 189±7 to 389±16 beats/min by minute 10 after both vagi were cut, this being followed by a decrease to 374±15, i.e., by 19 beats/min, 10 min later. In further tests on 11 pigeons injected with atropine

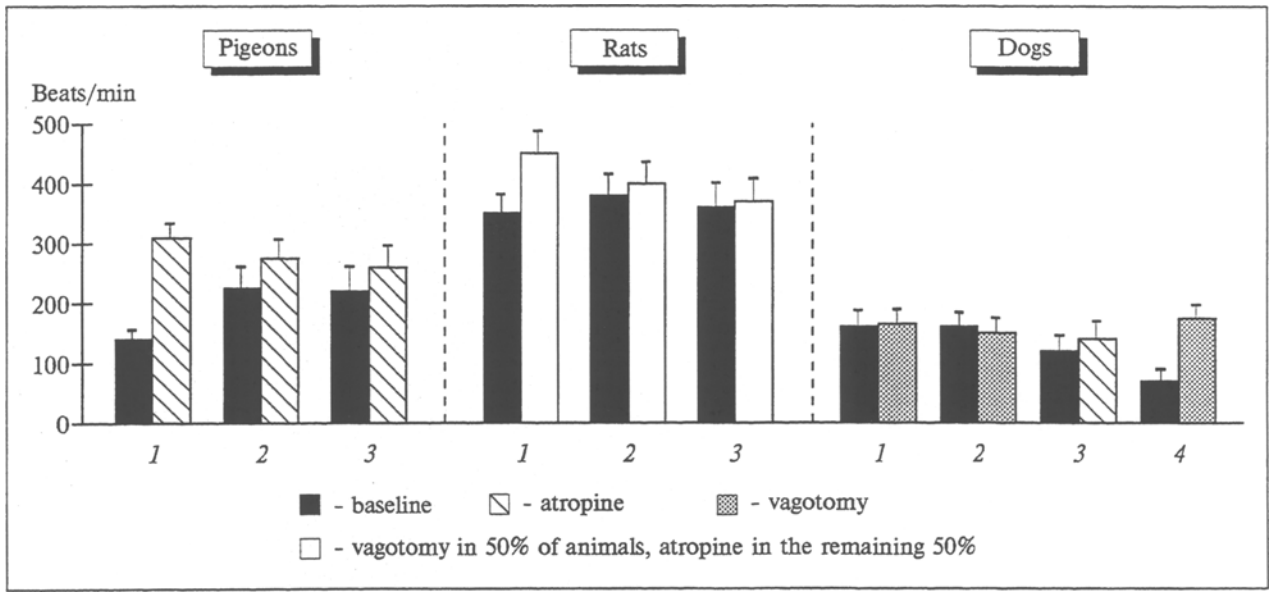

Fig. 3. Heart rates (HR) in pigeons, rats, and dogs under urethan (*1*), Hexenal (*2*), and Nembutal (*3*) anesthesia or under Hexenal or ether anesthesia with morphine premedication (*4*). *Black bars*: baseline; *hatched bars*: after bilateral vagotomy.

(2 mg/kg) 10 min after bilateral vagotomy, the heart rate dropped from 394±19 beats/min before atropine injection to 372±17 by minute 10 postinjection (i.e., by 22 beats/min), whereas in similar tests on 15 other pigeons, the heart rate remained virtually unchanged in the 10-20-minute interval postvagotomy (436±12 beats/min at minute 10 and 440±13 at minute 20), followed by a decrease to 425±13 beats/min over the next 10 min in the presence of atropine. These tests indicate that counting heart beats at different times after vagotomy yields conflicting results. In all instances, the tachycardia arising after the vagi were cut progressively decreased, even if the SNS was intact.

As noted above, one reason why the data from studies of vagal tone are contradictory may be the use of different types of anesthesia in different experiments. To check this possibility, we determined in pigeons the degree of vagotomy- and atropine-induced tachycardia under urethan, Hexenal, and Nembutal anesthesia and found that after atropine injection (2 mg/kg) the heart rate increased from 138±4 to 312±14 beats/min (by 126%) under urethan anesthesia ($p<0.001$; 14 pigeons), from 224±17 to 275±18 beats/min (by 23%) under Hexenal anesthesia ($p<0.05$; 20 pigeons), and by only 14% (from 219±19 to 249±16 beats/min) under Nembutal anesthesia ($p>0.2$; 21 pigeons). These findings indicate that the vagal tone is preserved under urethan, sharply decreased under Hexenal, and very weak under Nembutal anesthesia. Note that the background heart rates (i.e., before atropine injection) under Hexenal and Nembutal were much higher (224±17 and 219±19 beats/min, respectively) than under urethan (138±4 beats/min). It follows, then, that the different anesthetics have differential effects on the vagal tone. Under Nembutal, in particular, the vagal tone is extremely weak and erroneous conclusions are liable to be drawn unless this circumstance is taken into consideration. This thesis is supported by the results of our experiment with rats, in which the vagal tone was preserved only under urethan anesthesia: after the vagi were cut or blocked by atropine, the heart rate increased from the baseline value of 343±14 to 454±12 beats/min (by 32%, $p<0.001$; 23 rats); under Hexenal anesthesia (11 rats), it increased from 385±11 beats/min before vagotomy to 393±12 after it and under Nembutal anesthesia (8 rats), from 362±14 to 371±14 beats/min, respectively.

In the experiment with dogs, no postvagotomy tachycardia was observed under urethan (5 dogs), Hexenal (10 dogs), or Nembutal (5 dogs) anesthesia, the heart rate before and after vagotomy being 163±5 *vs.* 169±6, 161±7 *vs.* 155±7, and 119±4 *vs.* 146±5 beats/min, respectively. It was only in the dogs premedicated with morphine that the vagal tone was preserved regardless of whether the anesthesia was produced by Hexenal or by ether (the heart rate was 72±3 beats/min before vagotomy and 182±9 after it; $n=5$) (Fig. 3, *4*).

A significant effect on vagal tone may also be exerted by the depth of anesthesia. In a separate series of tests performed on pigeons under identical conditions (as regards the season and time of day and the period during which they had been kept in the vivarium), the heart rate after atropine

injection (2 mg/kg) increased from 133±2 to 354±53 beats/min (by 166%, $p<0.001$) in the 5 pigeons under surface anesthesia with urethan (1 g/kg) and from 193±21 to 352±25 beats/min (by 82%, $p<0.01$) in the 6 pigeons under general urethan anesthesia at the surgical stage, i.e., the degree of atropine-induced tachycardia in the latter pigeons was only half that in the former. This means that the depth of anesthesia is a factor having a strong effect on the experimental results and must be taken into account in order to avoid erroneous conclusions.

The results of this study lead us to conclude that the SNS does not participate in the development of postvagotomy tachycardia, which is exclusively due to suppression of the inhibitory vagal tone. The diminution or complete elimination and prevention of tachycardia observed in the experiments of some investigators was, as is attested by our findings, a consequence of interventions such as surgery and anesthesia (or the tachycardia just decreased in the course of time without these interventions) rather than a result of interruption of the sympathetic nerve supply. When the animal is in the resting state, the SNS does not affect the heart rate, which is entirely determined by the vagal tone and humoral substances circulating in the blood.

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